

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
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Hearing on “Examining the Federal response to the risks associated with per- and polyfluoroalkyl substances (PFAS)”

Testimony before the  
Senate Committee on Environment and Public Works

Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S.  
Director, National Institute of Environmental Health Sciences and National Toxicology Program  
National Institutes of Health

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Chairman Barrasso, Ranking Member Carper, Distinguished Members of the Senate Committee on Environment and Public Works, thank you for inviting me to testify at this hearing on a topic of increasing interest to the scientific community and to the greater public. I am Linda Birnbaum, the Director of the National Institute of Environmental Health Sciences (NIEHS) within the National Institutes of Health (NIH). I am also the Director of the National Toxicology Program (NTP), which serves to develop and coordinate toxicological testing across the Department of Health and Human Services, to conduct hazard assessments of toxic substances, and to manage the Interagency Coordinating Committee on the Validation of Alternative Methods. For the past 40 years I have conducted primary research in toxicology, and I am here today in my role as Director of NIEHS to provide a scientific perspective about the large, complex, and ever-expanding class of chemicals known as per and polyfluoroalkyl substances (PFAS).

### **The National Institute of Environmental Health Sciences (NIEHS)**

The NIEHS is one of several Federal agencies actively working to address various aspects related to PFAS. The NIEHS mission, as set forth under the Public Health Service Act, is to conduct and support research, training, and health information dissemination with respect to environmental factors that may affect human health, directly or indirectly.<sup>1</sup> With this mandate, NIEHS researchers use state-of-the-art science and technology to investigate the interplay between environmental exposures, human biology, genetics, and human disease to help prevent illness, morbidity, and mortality, and improve human health. No age group or disease is beyond the NIEHS mission. Considering this fact, NIEHS researchers collaborate with their peers at the other NIH Institutes and Centers focused on specific life stages, organ systems, or diseases.

NIEHS also has responsibilities under the Superfund Amendments and Reauthorization Act of 1986 (SARA) which created the Worker Training Program (WTP) and the Superfund Research Program (SRP) within NIEHS.<sup>2</sup> The SRP is a broad university-based research program capable of addressing the wide array of scientific uncertainties facing the national Superfund program. Within this purview is the development of methods and technologies to detect hazardous substances in the environment; advanced techniques for the detection, assessment, and evaluation of the effects on human health of hazardous substances; methods to assess the risks to human health presented by hazardous substances; and basic biological, chemical, and physical methods to reduce the amount and toxicity of hazardous substances.

For nearly three decades,<sup>3</sup> NIEHS has been the leading Federal agency sponsoring basic research investigating health effects associated with human exposures to PFAS. NIEHS-

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<sup>1</sup> Section 463 of the Public Health Service Act. ([42 USC 2851](#)).

<sup>2</sup> Sections 126(g) and 209(b) of the Superfund Amendments and Reauthorization Act of 1986. [Public Law 99-499](#), October 17, 1986. ([42 USC 9660a](#) and [42 USC 9660](#), respectively).

<sup>3</sup> Harris MW, Birnbaum LS. Developmental Toxicity of Perfluorodecanoic Acid in C57BL/6N Mice. *Fundam. Appl. Toxicol.* 1989; 12(3):442-448. DOI: [10.1093/toxsci/12.3.442](#).

supported research uses human observational studies, animal models, *in vitro* tissue and cell culture systems, *in silico* approaches, and high throughput screening to study the effects of environmental exposure.

The most conclusive research focuses on a single chemical to understand the cause and effect on human health. While studying potentially toxic chemicals, we are largely limited to natural history and population-based studies that attempt to find connections between populations exposed and health effects in the real world. For that reason, you will hear me talk about “associations” – certain health effects happened to more people than normal in populations that are exposed.

The research conducted to date reveals associations between PFAS exposures and a variety of specific adverse human health outcomes. These include the potential for effects on children’s cognitive and neurobehavioral development, immune system dysfunction, endocrine disruption, obesity, diabetes, lipid metabolism, and cancer. While knowledge about these epidemiologic associations has steadily expanded in recent years, many questions remain unanswered. The NIEHS and NTP, in coordination with other Federal agencies and State and local governments, continue to conduct research to enhance our understanding of the potential mechanisms and biological processes through which PFAS may be affecting human health. NIEHS coordinates and participates in governmental health research to assure applicability, disseminate findings, and prevent duplication of effort. To this end, NIEHS continues to co-host and participate in numerous symposia and collaborative working groups.

## **Per and Polyfluoroalkyl Substances (PFAS)**

Before detailing the health effects associated with PFAS exposures, it is necessary to describe this class of chemicals. First created in the 1930s and 1940s, PFAS include some 4,700 man-made chemicals that contain fluorine atoms bonded to a carbon chain.<sup>4</sup> The carbon-fluorine bond is one of the strongest ever created by man and is rarely seen in nature. The unique chemical composition of PFAS imparts desirable physical and chemical properties for consumer and industrial products, such as oil and water repellency, high and low temperature stability, and friction reduction. These properties have led to PFAS incorporation in a wide range of consumer products, including textiles, paper products, semiconductors, automotive and aerospace components, cookware, food packaging, and stain repellent clothing. In addition, PFAS play an important role in industrial processes and aqueous film-forming foams (AFFF) that are used as a firefighting tool.

Our scientific understanding of PFAS compounds stems almost entirely from studies on a select few. Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) have been manufactured the longest, are the most widespread in the environment, and are the most well-studied PFAS to date. PFOA was used in the production of fluoropolymers such as Teflon®, and PFOS in the production of the original line of Scotchgard® water repellent products. PFOA and PFOS are considered “long-chain” PFAS due to the length of their carbon chain

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<sup>4</sup> While approximately 4,700 fluorine-containing, man-made compounds have been created, not all of these compounds have entered into commerce or been actively used.

backbones and have been studied for several decades. A wide range of “short-chain” PFAS have been introduced recently as alternatives to the linear, “long-chain” compounds. All PFAS have garnered increased attention by both the scientific community and the public. Current efforts within the NIEHS and NTP to greatly enhance our understanding of additional long-chain as well as short-chain PFAS are detailed later in this testimony.

The chemical composition of PFAS impart high stability for product design, and this characteristic makes PFAS extremely stable in the environment. In fact, PFAS and complex PFAS degradation products remain in the environment for so long that scientists are unable to accurately estimate an environmental half-life. As PFAS are incorporated into more diverse processes and products, they have greater potential for release into the environment. Manufacturing and processing facilities, airports, and military installations that use firefighting foams are contributors to PFAS releases into the air, soil, and water, including both surface and groundwater sources of drinking water.<sup>5</sup> Because PFAS are resistant to environmental degradation processes, they are subject to long-range atmospheric and oceanic current transport. PFAS have been identified in both environmental and biological samples collected in some of the most remote areas on earth.

As new knowledge is acquired about the breadth of exposures in many communities and the potential hazards to human health, questions arise about whether continued use of PFAS in specific applications is necessary, or if alternatives exist that may be less harmful but still provide sufficient performance. As part of our portfolios, NIEHS and NTP contribute substantively to the field of alternatives assessment to ensure harmful chemicals are not replaced by similarly harmful but less well-studied related compounds.

## Human Exposures

Humans are exposed to PFAS through myriad pathways, practices, and products. Ingestion, particularly through drinking water, is the predominant human exposure pathway for many individuals or communities,<sup>6</sup> but recent studies suggest that other exposure pathways, including inhalation and dermal absorption, are significant for human exposure.<sup>7,8,9,10</sup> Some PFAS

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<sup>5</sup> Hu XC, Andrews DQ, Lindstrom AB, Bruton TA, Schaider LA, Grandjean P, Lohmann R, Carignan CC, Blum A, Balan SA, Higgins CP, Sunderland EM. Detection of Poly- and Perfluoroalkyl Substances (PFASs) in U.S. Drinking Water Linked to Industrial Sites, Military Fire Training Areas, and Wastewater Treatment Plants. *Environ. Sci. Technol. Lett.* 2016; 3(10):344-350. DOI: [10.1021/acs.estlett.6b00260](https://doi.org/10.1021/acs.estlett.6b00260).

<sup>6</sup> Agency for Toxic Substances and Disease Registry (ATSDR). Routes of Exposure and Health Effects. An Overview of Perfluoroalkyl and Polyfluoroalkyl Substances and Interim Guidance for Clinicians Responding to Patient Exposure Concerns. Interim Guidance. Revised on May 7, 2018. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Internet: [https://www.atsdr.cdc.gov/pfas/docs/pfas\\_clinician\\_fact\\_sheet\\_508.pdf](https://www.atsdr.cdc.gov/pfas/docs/pfas_clinician_fact_sheet_508.pdf).

<sup>7</sup> D’eon JC, Mabury SA. Is Indirect Exposure a Significant Contributor to the Burden of Perfluorinated Acids Observed in Humans? *Environ. Sci. Technol.* 2011; 45(19):7974–84. DOI: [10.1021/es200171y](https://doi.org/10.1021/es200171y).

<sup>8</sup> Schaider, LA, Balan, SA, Blum, A, Andrews, DQ, Strynar, M, Dickinson, ME, Lunderberg, DM, Lang, JR, Peaslee, GF. Fluorinated Compounds in U.S. Fast Food Packaging. *Environ. Sci. Technol. Lett.* 2017; 4(3):105-111. DOI: [10.1021/acs.estlett.6b00435](https://doi.org/10.1021/acs.estlett.6b00435).

<sup>9</sup> Franko J, Meade BJ, Frasch HF, Barbero AM, Anderson SE. Dermal Penetration Potential of Perfluorooctanoic Acid (PFOA) in Human and Mouse Skin. *J. Toxicol. Environ. Health A.* 2012; 75(1):50-62. DOI: <https://doi.org/10.1080/15287394.2011.615108>.

<sup>10</sup> Winkens K, Vestergren R, Berger U, Cousins IT. Early Life Exposure to Per- and Polyfluoroalkyl Substances

bioaccumulate, leading to concentrations in animals and humans that are significantly higher than the surrounding environment, and they enter the human food chain.<sup>11,12,13</sup>

Human exposures to PFAS are extremely widespread. The Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics' 2011–2012 U.S. National Health and Nutrition Examination Survey (NHANES) reported detectable PFAS blood serum concentrations in virtually all individuals (97 percent).<sup>14</sup> The most recent NHANES data indicate a reduction in serum concentrations of PFOS and PFOA since they were voluntarily phased out of production in the United States beginning in 2002 and 2006, respectively. Replacement PFAS have subsequently been rapidly introduced into the market and exposure is more difficult to assess accurately due to a lack of analytical standards.

## Health Effects Research

Our understanding of the health effects associated with PFAS and our ability to draw conclusions regarding the contribution of any specific PFAS to human disease is based on combined data from multiple studies investigating epidemiologic associations in human cohort studies, biological plausibility and pathways in animal studies, mechanistic effects in human tissue and cell culture systems, and rapid high-throughput screening. It is important to note that epidemiology studies alone cannot definitively prove causation, and while animal studies are an important marker of scientific discovery, they may not be perfect predictors of effects in humans. By combining and carefully considering data across multiple types of studies, we can begin to build an understanding of how PFAS impact human health and recommend steps to mitigate deleterious impacts.

When investigating possible human health effects of chemical compounds distributed in the environment, it is also important to recognize that effects from exposure to mixtures pose unique challenges. While studies indicate adverse health effects due to exposures from certain PFAS, such as PFOA and PFOS, we have only limited or no data on which to base conclusions for the majority of PFAS. Our current scientific method involves using our understanding of the biological and chemical processes being influenced by the few well-studied chemicals to extrapolate potential conclusions about structurally similar compounds which we can reasonably expect to act through the same pathways and have similar effects. More research is needed to identify causal relationships between exposure to PFAS and adverse health effects in

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(PFASs): a Critical Review. *Emerging Contaminants*. June 2017; (3)2:55-68. DOI: [10.1016/j.emcon.2017.05.001](https://doi.org/10.1016/j.emcon.2017.05.001).

<sup>11</sup> Bryne S, Seguinot-Medina S, Miller P, Waghiyi V, von Hippel FA, Loren Buck C, Carpenter DO. Exposure to Polybrominated Diphenyl Ethers and Perfluoroalkyl Substances in a Remote Population of Alaska Natives. 2017(Dec.); 231(1):387-395. *Environ. Poll.* DOI: [10.1016/j.envpol.2017.08.020](https://doi.org/10.1016/j.envpol.2017.08.020).

<sup>12</sup> Ghisi R, Vamerli T, Manzetti S. Accumulation of Perfluorinated Alkyl Substances (PFAS) in Agricultural Plants: A Review. *Environ. Res.* 2019(Feb.); 169:326-341. DOI: [10.1016/j.envres.2018.10.023](https://doi.org/10.1016/j.envres.2018.10.023).

<sup>13</sup> Scher DP, Kell JE, Huset CA, Barry KM, Hoffbeck RW, Yingling VL, Messing RB. Occurrence of Perfluoroalkyl Substances (PFAS) in Garden Produce at Homes with a History of PFAS-Contaminated Drinking Water. *Chemosphere*. 2018; 196:548-555. DOI: [10.1016/j.chemosphere.2017.12.179](https://doi.org/10.1016/j.chemosphere.2017.12.179).

<sup>14</sup> Hu XC, Andrews DQ, Lindstrom AB, Bruton TA, Schaidler LA, Grandjean P, Lohmann R, Carignan CC, Blum A, Balan SA, Higgins CP, Sunderland EM. Detection of Poly- and Perfluoroalkyl Substances (PFASs) in U.S. Drinking Water Linked to Industrial Sites, Military Fire Training Areas, and Wastewater Treatment Plants. *Environ. Sci. Technol. Lett.* 2016; 3(10):344-350. DOI: [10.1021/acs.estlett.6b00260](https://doi.org/10.1021/acs.estlett.6b00260).

humans.

### *Decreased Immune System Function*

As early as 1978, scientists observed immunotoxicity in non-human primates exposed to PFAS.<sup>15</sup> In 2016, NTP conducted a systematic literature review which concluded that PFOA and PFOS are presumed to be a hazard to healthy immune system function in humans.<sup>16</sup> This conclusion is based on a high level of evidence that PFOA and PFOS suppressed the antibody response in animal studies, and a moderate level of evidence that these chemicals affect multiple aspects of the immune system in humans. Adult PFAS exposure has also been associated with decreases in antibody production.<sup>17</sup> NTP is building on this 2016 systematic review to evaluate immunotoxicity of six related PFAS: PFDA, PFNA, PFHxA, PFBA, PFBS and PFHxS.<sup>18</sup>

### *Cancer*

The epidemiological data on associations between PFAS and cancer risk are limited. Those published studies were recently summarized by the Agency for Toxic Substances and Disease Registry (ATSDR) in their Draft Toxicological Profile for Perfluoroalkyls.<sup>19</sup> According to the Toxicological Profile, “Occupational and community exposure studies have found increases in the risk of testicular and kidney cancer associated with PFOA. No consistent epidemiologic evidence for other cancer types were found for PFOA.<sup>20,21</sup> For PFOS, one occupational exposure study reported an increase in bladder cancer,<sup>22</sup> but this was not supported by subsequent occupational studies. General population studies have not consistently reported increases in malignant tumors for PFOS. Epidemiologic studies examining other perfluoroalkyl compounds consisted of two case-control studies. No increases in breast cancer risk were observed for PFHxS or PFNA; an increased breast cancer risk was observed for PFOSA.<sup>23</sup>

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<sup>15</sup> Goldenthal EI, Jessup DC, Geil RG, Mehring JS. Final report, ninety day subacute rhesus monkey toxicity study, International Research and Development Corporation, study no. 137-090, November 10, 1978, U.S. EPA Administrative Record, AR226-0447.

<sup>16</sup> National Toxicology Program. Monograph on Immunotoxicity Associated with Exposures to PFOA and PFOS. Sept. 2016. Research Triangle Park, NC: U.S. Internet: <https://ntp.niehs.nih.gov/pubhealth/hat/noms/pfoa/index.html>.

<sup>17</sup> Kielsen K, Shamim Z, Ryder LP, Nielsen F, Grandjean P, Budtz-Jørgensen E, Heilmann C. Antibody Response to Booster Vaccination with Tetanus and Diphtheria in Adults Exposed to Perfluorinated Alkylates. *J. Immunotoxicol.* 2016; 13(2):270-3. DOI: [10.3109/1547691X.2015.1067259](https://doi.org/10.3109/1547691X.2015.1067259).

<sup>18</sup> The six PFAS for which the National Toxicology Program is building on its 2016 systematic review to evaluate immunotoxicity are: perfluorodecanoic acid (PFDA); perfluorononanoic acid (PFNA); perfluorohexanoic acid (PFHxA); perfluorobutanesulfonic acid (PFBS); perfluorobutanesulfonic acid (PFBS); and perfluorohexanesulfonic acid (PFHxS).

<sup>19</sup> Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for Perfluoroalkyls. (Draft for Public Comment). 2018. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Internet: <https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=1117&tid=237>.

<sup>20</sup> Barry V, Winqvist A, Steenland K. Perfluorooctanoic Acid (PFOA) Exposures and Incident Cancers Among Adults Living Near a Chemical Plant. *Environ. Health Perspect.* 2013; 121(11-12):1313-1318. DOI: [10.1289/ehp.1306615](https://doi.org/10.1289/ehp.1306615).

<sup>21</sup> Steenland K, Woskie S. Cohort Mortality Study of Workers Exposed to Perfluorooctanoic Acid. *Am. J. Epidemiol.* 2012; 176(10):909-917. DOI: [10.1093/aje/kws171](https://doi.org/10.1093/aje/kws171).

<sup>22</sup> Alexander BH, Olsen GW, Burris JM, Mandel JH, Mandel JS. Mortality of Employees of a Perfluorooctanesulphonyl Fluoride Manufacturing Facility. *Occup. Environ. Med.* 2003; 60:722-729. DOI: [10.1136/oem.60.10.722](https://doi.org/10.1136/oem.60.10.722).

<sup>23</sup> Bonefeld-Jørgensen EC, Long M, Fredslund SO, Bossi R, Olsen J. Breast Cancer Risk After Exposure to



Another case- control study did not find increases in prostate cancer for PFOA, PFOS, PFHxS, PFNA, PFDeA, or PFUA.<sup>24</sup> However, among men with a first-degree relative with prostate cancer, associations were found for PFOA, PFOS, PFHxS, PFDeA, and PFUA, but not for PFNA.”<sup>25</sup>

### *Child Development*

PFOA and PFOS cause developmental toxicity in animals.<sup>26,27,28</sup> Human epidemiology studies also show associations between some PFAS and developmental effects.<sup>29</sup> One human study found that PFAS exposure during pregnancy was associated with decreased birth weight and head circumference only in males.<sup>30</sup> Similar decreases in birth weight have been reported in rodents for over a decade.<sup>31</sup> Recent findings from NIEHS-supported epidemiological studies of a cohort of mothers and babies showed that prenatal exposure to PFOS is associated with cognitive effects and decreased ability to regulate behavior in school-age children. However, no similar association was observed in this study for PFOA exposure.<sup>32</sup>

A review of the epidemiological literature by an NIEHS-funded scientist summarized findings from several prospective cohorts on the relationship between prenatal exposure to certain PFAS and neurodevelopmental and neurobehavioral outcomes – for example, cognitive abilities, psychomotor development, attention-deficit hyperactivity disorder, and cerebral palsy. So far, the available body of evidence is inconsistent with respect to these associations, both with respect to which compounds may have adverse effects and timing of potential windows of vulnerability. Additional studies are needed to resolve these questions.<sup>33</sup> Animal

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Perfluorinated Compounds in Danish Women: A Case-Control Study Nested in The Danish National Birth Cohort. *Cancer Causes Control*. 2014; 25(11):1439-1448. DOI: [10.1007/s10552-014-0446-7](https://doi.org/10.1007/s10552-014-0446-7).

<sup>24</sup> Hardell E, Karrman A, van Bavel B, Bao J, Carlberg M, Hardell L. Case-Control Study on Perfluorinated Alkyl Acids (PFAAs) and the Risk of Prostate Cancer. *Environ. Int.* 2014; 63:35-39. DOI: [10.1016/j.envint.2013.10.005](https://doi.org/10.1016/j.envint.2013.10.005).

<sup>25</sup> Ibid.

<sup>26</sup> White SS, Calafat AM, Kuklenyik Z, Thibodeaux J, Wood C, Fenton, SE. Gestational PFOA Exposure of Mice Is Associated with Altered Mammary Gland Development in Dams and Female Offspring. *Toxicol. Sci.* 2007; 96(1):133-144. DOI: [10.1093/toxsci/kfl177](https://doi.org/10.1093/toxsci/kfl177).

<sup>27</sup> Butenhoff JL, Ehresman DJ, Chang SC, Parker GA, Stump DG. Gestational and Lactational Exposure to Potassium Perfluorooctanesulfonate (K+PFOS) in Rats: Developmental Neurotoxicity. *Reprod. Toxicol.* 2009 Jun; 27(3-4):319-30. DOI: [10.1016/j.reprotox.2008.12.010](https://doi.org/10.1016/j.reprotox.2008.12.010).

<sup>28</sup> Chen T, Zhang L, Yue JQ, Lv ZQ, Xia W, Wan YJ, Li YY, Xu SQ. Prenatal PFOS Exposure Induces Oxidative Stress and Apoptosis in the Lung of Rat Off-Spring. *Reprod. Toxicol.* 2012 Jul; 33(4):538-45. DOI: [10.1016/j.reprotox.2011.03.003](https://doi.org/10.1016/j.reprotox.2011.03.003).

<sup>29</sup> White SS, Fenton SE, Hines EP. Endocrine Disrupting Properties of Perfluorooctanoic Acid. *J. Steroid Biochem. Mol. Biol.* 2011 Oct; 127(1-2):16–26. DOI: [10.1016/j.jsbmb.2011.03.011](https://doi.org/10.1016/j.jsbmb.2011.03.011).

<sup>30</sup> Valvi D, Oulhote Y, Weihe P, Dalgård C, Bjerve KS, Steuerwald U, Grandjean P. Gestational Diabetes and Offspring Birth Size at Elevated Environmental Pollutant Exposures. *Environ. Int.* 2017 Oct; 107:205-215. DOI: [10.1016/j.envint.2017.07.016](https://doi.org/10.1016/j.envint.2017.07.016).

<sup>31</sup> Hines, EP, White, SS, Stanko, JP, Gibbs-Flournoy JE, Lau C, Fenton SE. Phenotypic Dichotomy Following Developmental Exposure to Perfluorooctanoic Acid (PFOA) in Female CD-1 Mice: Low Doses Induce Elevated Serum Leptin and Insulin, and Overweight in Mid-Life. *Mol. Cell. Endocrinol.* 2009 May 25; 304(1-2):97-105. DOI: [10.1016/j.mce.2009.02.021](https://doi.org/10.1016/j.mce.2009.02.021).

<sup>32</sup> Vuong AM, Yolton K, Webster GM, Sjödin A, Calafat AM, Braun JM, Dietrich KN, Lanphear BP, Chen A. Prenatal Polybrominated Diphenyl Ether and Perfluoroalkyl Substance Exposures and Executive Function in School-Age Children. *Environ. Res.* 2016 May; 147:556–564. DOI: [10.1016/j.envres.2016.01.008](https://doi.org/10.1016/j.envres.2016.01.008).

<sup>33</sup> Braun J. Early-Life Exposure to EDCs: Role in Childhood Obesity and Neurodevelopment. *Nat. Rev. Endocrinol.* 2017 Mar; 13(3):161–173. DOI: [10.1038/nrendo.2016.186](https://doi.org/10.1038/nrendo.2016.186).

studies are consistent with and provide additional biological plausibility for the developmental effects observed in the human studies.<sup>34,35</sup>

### *Endocrine Disruption*

Studies suggest that some PFAS may interfere with healthy hormonal function in the body. Our endocrine system controls our basic physiology, including metabolism, growth, fertility, and development. Human studies suggest a concern that early-life exposures to some PFAS may contribute to altered insulin resistance.<sup>36,37</sup> Although further confirmation is required, the findings from one study suggest that exposures to some PFAS during pregnancy may influence lipid metabolism and glucose tolerance.<sup>38</sup> A study of pregnant women in Cincinnati found that those with higher prenatal PFAS levels had children with higher body fat levels at age eight<sup>39</sup>—a finding reinforced by other epidemiological studies<sup>40,41</sup> and similar effects on excessive body weight gain reported for experimental animals.<sup>42</sup> It appears that some PFAS may also affect body weight later in life. Scientists at the Harvard School of Public Health have found that adults with higher blood levels of some PFAS have lower resting metabolic rates, meaning they burn fewer calories while resting, which makes it difficult for them to maintain weight loss.<sup>43</sup>

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<sup>34</sup> Valvi D, Oulhote Y, Weihe P, Dalgård C, Bjerve KS, Steuerwald U, Grandjean P. Gestational diabetes and offspring birth size at elevated environmental pollutant exposures. *Environ. Int.* 2017 Oct; 107:205-215. DOI: [10.1016/j.envint.2017.07.016](https://doi.org/10.1016/j.envint.2017.07.016).

<sup>35</sup> Hines EP, White SS, Stanko JP, Gibbs-Flournoy EA, Lau C, Fenton SE. Phenotypic dichotomy following developmental exposure to perfluorooctanoic acid (PFOA) in female CD-1 mice: Low doses induce elevated serum leptin and insulin, and overweight in mid-life. *Mol Cell Endocrinol.* 2009 May; 304(1-2):97-105. DOI: [10.1016/j.mce.2009.02.021](https://doi.org/10.1016/j.mce.2009.02.021).

<sup>36</sup> Donat-Vargas C, Bergdahl IA, Tornevi A, Wennberg M, Sommar J, Kiviranta H, Koponen J, Rolandsson O, Åkesson A. Perfluoroalkyl Substances and Risk of Type II Diabetes: A Prospective Nested Case-Control Study. *Environ. Int.* 2019 Feb; 123:390-398. DOI: [10.1016/j.envint.2018.12.026](https://doi.org/10.1016/j.envint.2018.12.026).

<sup>37</sup> Fleisch AF, Rifas-Shiman SL, Mora AM, Calafat AM, Ye X, Luttmann-Gibson H, Gillman MW, Oken E, Sagiv SK. Early-Life Exposure to Perfluoroalkyl Substances and Childhood Metabolic Function. *Environ. Health Perspect.* 2017 Mar; 125(3):481-487. DOI: [10.1289/EHP303](https://doi.org/10.1289/EHP303).

<sup>38</sup> Matilla-Santander N, Valvi D, Lopez-Espinosa MJ, Manzano-Salgado CB, Ballester F, Ibarluzea J, Santa-Marina L, Schettgen T, Guxens M, Sunyer J, Vrijheid M. Exposure to Perfluoroalkyl Substances and Metabolic Outcomes in Pregnant Women: Evidence from the Spanish INMA Birth Cohorts. *Environ. Health Perspect.* 2017 Nov 13; 125(11):117004. DOI: [10.1289/EHP1062](https://doi.org/10.1289/EHP1062).

<sup>39</sup> Braun JM, Chen A, Romano ME, Calafat AM, Webster GM, Yolton K, Lanphear BP. Prenatal Perfluoroalkyl Substance Exposure and Child Adiposity at 8 Years of Age: The HOME Study. *Obesity.* 2016 Jan; 24(1):231-7. DOI: [10.1002/oby.21258](https://doi.org/10.1002/oby.21258).

<sup>40</sup> Mora AM, Oken E, Rifas-Shiman SL, Webster TF, Gillman MW, Calafat AM, Ye X, Sagiv SK. Prenatal Exposure to Perfluoroalkyl Substances and Adiposity in Early and Mid-Childhood. *Environ. Health Perspect.* 2017 Mar; 125(3):467-473. DOI: [10.1289/EHP246](https://doi.org/10.1289/EHP246).

<sup>41</sup> Karlsen M, Grandjean P, Weihe P, Steuerwald U, Oulhote Y, Valvi D. Early-Life Exposures to Persistent Organic Pollutants in Relation to Overweight in Preschool Children. *Reprod. Toxicol.* 2017 Mar; 68:145-153. DOI: [10.1016/j.reprotox.2016.08.002](https://doi.org/10.1016/j.reprotox.2016.08.002).

<sup>42</sup> Hines EP, White SS, Stanko JP, Gibbs-Flournoy EA, Lau C, Fenton SE. Phenotypic Dichotomy Following Developmental Exposure to Perfluorooctanoic Acid (PFOA) in Female CD-1 Mice: Low Doses Induce Elevated Serum Leptin and Insulin, and Overweight in Mid-Life. *Mol. Cell. Endocrinol.* 2009 May 25; 304(1-2):97-105. DOI: [10.1016/j.mce.2009.02.021](https://doi.org/10.1016/j.mce.2009.02.021).

<sup>43</sup> Liu G, Dhana K, Furtado JD, Rood J, Zong G, Liang L, Qi L, Bray GA, DeJonge L, Coull B, Grandjean P, Sun Q. Perfluoroalkyl Substances and Changes in Body Weight and Resting Metabolic Rate in Response to Weight-Loss Diets: A Prospective Study. *PLoS Med.* 2018; 15(2):e1002502. DOI: [10.1371/journal.pmed.1002502](https://doi.org/10.1371/journal.pmed.1002502).



Effects on weight gain have been seen in numerous animal studies,<sup>44,45,46</sup> supporting this association in humans. It is particularly concerning that some PFAS alter thyroid hormone homeostasis that regulates metabolism and growth.<sup>47,48,49</sup>

Fertility is another outcome related to endocrine effects. A literature review of recent human epidemiologic evidence on the association between exposure to some PFAS and measures of human fertility show effects on the probability of conception.<sup>50,51</sup> In addition, several recent studies have shown that the duration of breastfeeding decreases with increasing blood concentrations of certain PFAS.<sup>52,53</sup> This is similar to 2006 findings in animals reporting impaired mammary gland development and lactation during and after pregnancy in mice.<sup>54</sup>

## NIEHS Extramural PFAS Research Portfolio

NIEHS currently funds over 40 academic-based research projects that explore the health consequences of PFAS exposures. These projects include fundamental and human-based research projects that are funded through competitive awards using various NIH grant mechanisms. Concomitant with the recent emergence of public concerns about PFAS exposures, NIEHS has received a large increase in the number of grant applications and awarded more grants in this research area over the past year. For example, since September 2018, NIEHS has

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<sup>44</sup> Grün F, Blumberg B. Endocrine Disruptors as Obesogens. *Mol. Cell. Endocrinol.* 2009 May 25; 304(1-2):19-29. DOI: [10.1016/j.mce.2009.02.018](https://doi.org/10.1016/j.mce.2009.02.018).

<sup>45</sup> Shi Z, Zhang H, Ding L, Feng Y, Xu M, Dai J. The Effect of Perfluorododecanonic Acid on Endocrine Status, Sex Hormones and Expression of Steroidogenic Genes in Pubertal Female Rats. *Reprod. Toxicol.* 2009 Jun; 27(3-4):352-9. DOI: [10.1016/j.reprotox.2009.02.008](https://doi.org/10.1016/j.reprotox.2009.02.008).

<sup>46</sup> Holtcamp W. Obesogens: An Environmental Link to Obesity. *Environ. Health. Perspect.* 2012; 120:a62-8. DOI: [10.1289/ehp.120-a62](https://doi.org/10.1289/ehp.120-a62).

<sup>47</sup> Byrne SC, Miller P, Seguinot-Medina S, Waghiyi V, Buck CL, von Hippel FA, Carpenter DO. Exposure to Perfluoroalkyl Substances and Associations with Serum Thyroid Hormones in a Remote Population of Alaska Natives. *Environ. Res.* 2018 Oct; 166:537-543. DOI: [10.1016/j.envres.2018.06.014](https://doi.org/10.1016/j.envres.2018.06.014).

<sup>48</sup> Kim MJ, Moon S, Oh BC, Jung D, Ji K, Choi K, Park YJ. Association Between Perfluoroalkyl Substances Exposure and Thyroid Function in Adults: A Meta-Analysis. *PLoS One.* 2018 May 10; 13(5):e0197244. DOI: [10.1371/journal.pone.0197244](https://doi.org/10.1371/journal.pone.0197244).

<sup>49</sup> Preston EV, Webster TF, Oken E, Claus Henn B, McClean MD, Rifas-Shiman SL, Pearce EN, Braverman LE, Calafat AM, Ye X, Sagiv SK. Maternal Plasma per- and Polyfluoroalkyl Substance Concentrations in Early Pregnancy and Maternal and Neonatal Thyroid Function in a Prospective Birth Cohort: Project Viva (USA). *Environ. Health. Perspect.* 2018 Feb 27; 126(2):027013. DOI: [10.1289/EHP2534](https://doi.org/10.1289/EHP2534).

<sup>50</sup> Bach CC, Vested A, Jørgensen K, Bonde JP, Henriksen TB, Toft G. Perfluoroalkyl and Polyfluoroalkyl Substances and Measures of Human Fertility: A Systematic Review. *Crit. Rev. Toxicol.* 2016 Oct; 46(9):735-55. DOI: [10.1080/10408444.2016.1182117](https://doi.org/10.1080/10408444.2016.1182117).

<sup>51</sup> Jørgensen KT, Specht IO, Lenters V, Bach CC, Rylander L, Jönsson BAG, Lindh CH, Giwercman A, Heederik D, Toft G, Bonde JP. Perfluoroalkyl substances and time to pregnancy in couples from Greenland, Poland and Ukraine. *Environmental Health.* 2014; 13:116. DOI: [10.1186/1476-069X-13-116](https://doi.org/10.1186/1476-069X-13-116).

<sup>52</sup> Timmermann CA, Budtz-Jørgensen E, Petersen MS, Weihe P, Steuerwald U, Nielsen F, Jensen TK, Grandjean P. Shorter Duration of Breastfeeding at Elevated Exposures to Perfluoroalkyl Substances. *Reprod. Toxicol.* 2017 Mar; 68:164-170. DOI: [10.1016/j.reprotox.2016.07.010](https://doi.org/10.1016/j.reprotox.2016.07.010).

<sup>53</sup> Romano ME, Xu Y, Calafat AM, Yolton K, Chen A, Webster GM, Eliot MN, Howard CR, Lanphear BP, Braun JM. Maternal Serum Perfluoroalkyl Substances During Pregnancy and Duration of Breastfeeding. *Environ. Res.* 2016 Aug; 149:239-246. DOI: [10.1016/j.envres.2016.04.034](https://doi.org/10.1016/j.envres.2016.04.034).

<sup>54</sup> White SS, Calafat AM, Kuklennyik Z, Villanueva L, Zehr RD, Helfant L, Strynar MJ, Lindstrom AB, Thibodeaux JR, Wood C, Fenton SE. Gestational PFOA Exposure of Mice is Associated with Altered Mammary Gland Development in Dams and Female Offspring. *Toxicol. Sci.* 2007 Mar; 96(1):133-44. DOI: [10.1093/toxsci/kfl177](https://doi.org/10.1093/toxsci/kfl177).

awarded 10 new research project grants—representing a more than 30% increase in its extramural PFAS portfolio—focused on PFAS, many of which are investigating early life exposures (*in utero* and early childhood) and long-term health effects. Moreover, over the past seven months (September 2018-March 2019), NIEHS grantees have published 28 manuscripts detailing the health impacts of PFAS exposures. This list of manuscripts is attached to my testimony.

### **NIEHS Superfund Research Program (SRP)**

Recently, NIEHS competitively awarded a five-year grant to the University of Rhode Island to fund its “Sources, Transport, Exposure and Effects of PFASs (STEEP) Superfund Research Program Center” (Fiscal Years 2017-2022).<sup>55</sup> The Center is assessing the impact of PFAS exposures on immune dysfunction and metabolic abnormalities by examining the health of nine-year-old children from birth cohorts in the Faroe Islands (Denmark).<sup>56</sup> Recent results from a prospective study of over 1,000 children show that weakened immune response is correlated with PFAS exposure.<sup>57</sup> The Center is also tracing unique PFAS chemical fingerprints at a contaminated groundwater site on Cape Cod, Massachusetts, leading to exposure through drinking water, as a function of PFAS chemistry, geochemistry, and distance from the source. Additionally, the Center is developing and validating novel passive sampling tools for PFAS to measure time weighted average concentrations for some PFAS and their volatile precursors. These tools can be deployed to aid site managers in their risk characterization.<sup>58</sup> Promising results to date indicate that these sampling tools can be effective monitors for airborne PFAS, a route that may contribute significantly to PFAS fate, transport, and human exposure. Finally, the Center is engaging communities and advising stakeholders on ways to effectively reduce human exposure to PFAS. Other NIEHS Superfund Research Program Centers are providing technical assistance regarding PFAS to State and local governments, water authorities, and private well users. The Brown University Superfund Research Center has developed Geographical Information Systems (GIS)-based databases for identifying municipalities at risk for PFAS exposure based on past land use data.<sup>59,60</sup> Other research at the University of Arizona is also developing groundwater modeling tools to predict how PFAS move in the subsurface, helping to

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<sup>55</sup> NIH Grant No. P42ES027706. Sources, Transport, Exposure and Effects of PFASs (STEEP). McCann, Alyson. University of Rhode Island. Awarded August 30, 2017. [NIH RePORTER Link](#).

<sup>56</sup> Dassuncao C, Pickard H, Pfohl M, Tokranov AK, Li M, Mikkelsen B, Slitt A, Sunderland EM. Phospholipid Levels Predict the Tissue Distribution of Poly- and Perfluoroalkyl Substances in a Marine Mammal. *Environ. Sci Technol. Lett.* 2019; 6(3):119-125. DOI: [10.1021/acs.estlett.9b00031](#).

<sup>57</sup> Budtz-Jørgensen E, Grandjean P. Application of Benchmark Analysis for Mixed Contaminant Exposures: Mutual Adjustment of Perfluoroalkylate Substances Associated with Immunotoxicity. *PLoS One.* 2018; 13(10):e0205388. DOI: [10.1371/journal.pone.0205388](#).

<sup>58</sup> Dixon-Anderson E, Lohmann R. Field-Testing Polyethylene Passive Samplers for the Detection of Neutral Polyfluorinated Alkyl Substances in Air and Water. *Environ. Toxicol. Chem.* 2018; 37:3002-3010. DOI: [10.1002/etc.4264](#).

<sup>59</sup> Guelfo J, Adamson DT. Evaluation of a National Data Set for Insights into Sources, Composition, and Concentrations of Per- and Polyfluoroalkyl Substances (PFASs) in U.S. Drinking Water. *Environ. Pollut.* 2018; 236:505-513. DOI: [10.1016/j.envpol.2018.01.066](#).

<sup>60</sup> Guelfo J, Marlow T, Klein D, Savitz D, Frickel S, Crimi M, Suuberg EM. Evaluation and Management Strategies for Per- and Polyfluoroalkyl Substances (PFASs) in Drinking Water Aquifers: Perspectives from Impacted U.S. Northeast Communities. *Environ. Health Perspect.* 2018; 126:13. DOI: [10.1289/ehp2727](#).

understand where to target remediation approaches.<sup>61,62,63,64</sup> SRP grantees have continued to work closely with Federal and State officials to translate scientifically defensible findings to guide best practices for PFAS monitoring and management—including several outreach efforts within regions impacted by PFAS—such as the New England States (Northeast Waste Management Officials’ Association), as well as Michigan, North Carolina and New York. These outreach efforts also extend to communities grappling with the complexities of PFAS exposure and the uncertainties of risk.

The Superfund Research Program has been a key player in developing new solutions to PFAS contamination. Through Small Business Innovation Research (SBIR) grants, the Program provides support to scientists and engineers developing novel technologies for mitigation and remediation of PFAS in the environment. NIEHS SBIR grantee CycloPure, Inc., is developing novel, high-affinity cyclodextrin polymers for the cost-effective remediation of PFAS from water.<sup>65</sup> In another NIEHS SBIR project, EnChem Engineering, Inc. is developing and demonstrating an innovative combined *in-situ* / *ex-situ* technology to cost-effectively expedite treatment of PFAS at Superfund sites. The technology includes a mobile unit that combines a wash cycle using a non-toxic sugar, followed by an intense extraction and destruction process. Their results show more than 99% removal.<sup>66</sup> Yet another *in-situ* / *ex-situ* process is being developed by Lynntech, Inc. and utilizes plasma-based technology to decompose PFAS in water.<sup>67</sup> Additionally, the Michigan State University and Texas A&M University Superfund Research Centers are developing strategies to remediate PFAS via energy efficient nanoreactors capable of breaking the carbon-fluorine bond, as well as hydrogel sorbents to extract PFAS, respectively.<sup>68,69,70</sup> Also of note, the University of California, Berkeley Superfund Research

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<sup>61</sup> NIH Grant No. P42ES004940. Sequestration Processes for Attenuation and Treatment of Arsenic and Other Toxic Elements in Mine Waters. Brusseau, Mark. University of Arizona. Awarded August 1, 2017. [NIH RePORTER Link](#).

<sup>62</sup> Brusseau ML. The Influence of Molecular Structure on the Adsorption of PFAS to Fluid-Fluid Interfaces: Using QSPR to Predict Interfacial Adsorption Coefficients. *Water Res.* 2019; 152:148-158. DOI: [10.1016/j.watres.2018.12.057](#).

<sup>63</sup> Brusseau ML. Assessing the Potential Contributions of Additional Retention Processes to PFAS Retardation in the Subsurface. *Sci. Total Environ.* 2018; 613:176-185. DOI: [10.1016/j.scitotenv.2017.09.065](#).

<sup>64</sup> Brusseau M, Yan N, Van Glubt S, Wang Y, Chen W, Lyu Y, Dungan B, Carroll K, Holguin FO. Comprehensive Retention Model for PFAS Transport in Subsurface Systems. *Water Res.* 2019; 148:41-50. DOI: [10.1016/j.watres.2018.10.035](#).

<sup>65</sup> NIH Grant No. R43ES029401. Remediation of Perfluorinated Chemicals in Water Using Novel High-Affinity Polymer Adsorbents. Barin, Gokhan. CycloPure, Inc. Awarded March 22, 2018. [NIH RePORTER Link](#).

<sup>66</sup> NIH Grant No. R43ES028649. Bench Scale Studies of Novel In-situ Aquifer Remediation of Recalcitrant Fluorinated Organic Compounds at Superfund Sites. Ball, Raymond. EnChem Engineering, Inc. Awarded August 28, 2017. [NIH RePORTER Link](#).

<sup>67</sup> NIH Grant No. R43ES030250. Continuous Removal/Disposal System for the Concurrent Sorption and Breakdown of Contaminants into Harmless Precipitates. Miller, Joseph. Lynntech, Inc. Awarded September 18, 2018. [NIH RePORTER Link](#).

<sup>68</sup> NIH Grant No. P42ES027704. Mitigation of Chemical and Mixture Effects Through Broad-Acting Sorbents. Phillips, Timothy. Texas A&M University. Awarded August 31, 2017. [NIH RePORTER Link](#).

<sup>69</sup> Huang PJ, Hwangbo M, Chen ZY, Liu YN, Kameoka J, Chu KH. Reusable Functionalized Hydrogel Sorbents for Removing Long- and Short-Chain Perfluoroalkyl Acids (PFAAs) and GenX from Aqueous Solution. *ACS Omega.* 2018; 3(12):17447–17455. DOI: [10.1021/acsomega.8b02279](#).

<sup>70</sup> Tian H, Gao J, Li H, Boyd SA, Gu C. Complete Defluorination of Perfluorinated Compounds by Hydrated Electrons Generated from 3-Indole-acetic-acid in Organomodified Montmorillonite. *Sci. Rep.* 2016; 6:32949. DOI:

Center is combining biological and chemical treatment options to degrade and destroy PFAS and AFFF.<sup>71,72,73</sup>

### **NIEHS Time-Sensitive Research Awards**

In addition to its regular funding programs, NIEHS has used a mechanism to support time-sensitive research opportunities related to PFAS. Time-sensitive grants are a rapid mechanism used to support research that characterizes initial exposures, collects human biological samples, and collects human health and exposure data.<sup>74</sup> Researchers at the Colorado School of Public Health, the University of Colorado Anschutz Medical Campus, and the Colorado School of Mines are studying PFAS exposures in residents near Colorado Springs whose wells and public water systems were contaminated with a wide range of PFAS, including high levels of perfluorohexane sulfonate (PFHxS).<sup>75,76</sup> This time-sensitive study started near the peak of exposure after contamination was discovered and will explore ways to measure how exposure levels to PFAS in the residents change over time.

In 2016, elevated levels of GenX, a short-chain PFAS containing an ether link generated in the production of non-stick coatings, were detected in North Carolina's Cape Fear River. The Cape Fear River provides drinking water for approximately 300,000 people and a production facility had been releasing GenX upstream. NIEHS funded a study at North Carolina State University to address community questions about GenX exposure and health effects, including GenX's potential toxicity, how it is stored in the body, and how long it remains in the environment.<sup>77,78</sup> Sampling results to date indicate elevation of GenX above the North Carolina Department of Health and Human Services health goal—140 parts per trillion—in treated water from at least

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[10.1038/srep32949](https://doi.org/10.1038/srep32949).

<sup>71</sup> Bruton TA, Sedlak DL. Treatment of Aqueous Film-Forming Foam by Heat-Activated Persulfate Under Conditions Representative of In Situ Chemical Oxidation. *Environ. Sci. Technol.* 2017; 51:13878-13885. DOI: [10.1021/acs.est.7b03969](https://doi.org/10.1021/acs.est.7b03969).

<sup>72</sup> Bruton TA, Sedlak DL. Treatment of Perfluoroalkyl Acids by Heat-Activated Persulfate Under Conditions Representative of In Situ Chemical Oxidation. *Chemosphere.* 2018; 206:457-464. DOI: [10.1016/j.chemosphere.2018.04.128](https://doi.org/10.1016/j.chemosphere.2018.04.128).

<sup>73</sup> Yi S, Harding-Marjanovic KC, Houtz EF, Gao Y, Lawrence JE, Nichiporuk RV, Iavarone A, Zhuang W, Field JA, Sedlak DL, Alvarez-Cohen L. Biotransformation of AFFF Component 6:2 Fluorotelomer Thioether Amido Sulfonate Generates 6:2 Fluorotelomer Thioether Carboxylate Under Sulfate-Reducing Conditions. *Environ. Sci. Technol. Lett.* 2018; 5:283-288. DOI: [10.1021/acs.estlett.8b00148](https://doi.org/10.1021/acs.estlett.8b00148).

<sup>74</sup> National Institute of Environmental Health Sciences. Time-Sensitive Research Opportunities in Environmental Health. Internet: <https://www.niehs.nih.gov/research/supported/timesensitive/index.cfm>.

<sup>75</sup> NIH Grant No. R21ES029394. Exposure and Health Effects from Poly- and Perfluoroalkyl Substances in Colorado Water. Adgate, John L. University of Colorado Denver. Awarded December 13, 2017. [NIH RePORTER Link](#).

<sup>76</sup> Gill N. Exposure Study to Assess People and Water Near Colorado Springs; Toxic Chemicals Have Contaminated Water Supplies for 65,000. *CU Anschutz Today*. December 21, 2017. Internet: <https://www.cuanschutztoday.org/exposure-study-assess-people-water-near-colorado-springs>.

<sup>77</sup> NIH Grant No. R21ES029353. Assessing Impact of Drinking Water Exposure to GenX (Hexafluoropropylene Oxide Dimer Acid) in the Cape Fear River Basin, North Carolina. Hoppin, Jane. North Carolina State University Raleigh. Awarded on October 31, 2017. [NIH RePORTER Link](#).

<sup>78</sup> Peake T. Researchers Receive Grant to Study GenX Exposure in New Hanover County Residents. *NC State News*. November 1, 2017. Internet: <https://news.ncsu.edu/2017/11/genx-study/>.

one water treatment plant,<sup>79</sup> and groundwater-fed drinking water wells without granular activated carbon filtration.<sup>80</sup> Many other PFAS were also measured in treated Cape Fear River tap water. GenX was not detected in the tap water of homes whose groundwater was treated with granular activated carbon filtration. Blood and urine levels reported to date as part of this ongoing analysis reveal that PFOA, PFOS, and additional known and unknown PFAS have been detected in the study population. In rodent models, NTP is studying how GenX moves through the body and whether it affects function of the placenta, immune system, liver, and other tissues.

## **NTP REACT Program**

The NTP Responsive Evaluation and Assessment of Chemical Toxicity, or REACT, Program is broadening our understanding of PFAS by studying over a hundred compounds that fall into different subclasses based on similarities in chemical properties. Scientists will be able to compare one PFAS to another, determine the relationship between chain length and other structural features and toxicity, and inform on whether there are common or overlapping patterns of toxicity.

REACT uses a combination of approaches. One project analyzes the chemical structure of PFAS compounds to see what information is available in databases for that compound or others with similar structure. Chemical structure plays a major role in how chemicals interact and chemicals with similar structure often have similar toxicity. This computer-based step is known as *in silico* screening. Based on *in silico* results, chemicals can be selected for further targeted laboratory testing with cells, known as *in vitro* testing. Examples include testing whether PFAS cause cells to die or substantially alter the function of human liver, placenta, or mammary gland derived cells. Some of these tests are similar to, or a refinement of, those used in the automated Toxicology in the 21st Century (Tox21) Program, a Federal collaboration among the NIH, the U.S. Environmental Protection Agency (EPA), and the U.S. Food and Drug Administration (FDA).<sup>81</sup> The *in vitro* data are then examined to prioritize select chemicals for toxicity testing in animals, known as *in vivo* studies, so the data can be considered all together. REACT is a collaborative program with EPA. Both NTP and EPA are contributing complementary resources to coordinate and share what is learned about individual chemicals.

## **Current Challenges**

Real-world human exposures to PFAS involve complex mixtures, not individual chemicals. This fact complicates both the science of exposure and the assessment of health risks.<sup>82</sup> Currently, analytical techniques are limited for determining which specific PFAS are contained in a given

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<sup>79</sup> North Carolina Department of Environmental Quality. GenX Results. Internet: <https://www.ncwater.org/?page=690&Action=doGraphs>.

<sup>80</sup> Leonard L. North Carolina Department of Environmental Quality. Latest test results show elevated levels of GenX in 30 more private wells. December 13, 2017. Internet: <https://deq.nc.gov/news/press-releases/2017/12/13/latest-test-results-show-elevated-levels-genx-30-more-private-wells>.

<sup>81</sup> U.S. Environmental Protection Agency. Toxicology Testing in the 21st Century (Tox21). Internet: <https://www.epa.gov/chemical-research/toxicology-testing-21st-century-tox21>.

<sup>82</sup> Kotthoff M, Bücking M. Four Chemical Trends Will Shape the Next Decade's Directions in Perfluoroalkyl and Polyfluoroalkyl Substances Research. *Front. Chem.* 2018 Apr 5; 6:103. DOI: [10.3389/fchem.2018.00103](https://doi.org/10.3389/fchem.2018.00103).



complex mixture. Further, toxicological information on these combined PFAS mixtures remains incomplete. Additional research is needed to assess environmental exposures to mixtures and determine their combined effects.

Apart from the challenge of characterizing PFAS in environmental samples is the challenge of studying PFAS in the human body. Our present understanding is that the time required for elimination of PFAS from the human body can vary. While some longer chain molecules may remain in the blood for years, shorter chain PFAS may be more quickly eliminated. Differences in elimination rates of longer and shorter chain PFAS complicates biomonitoring as well as toxicological studies. However, lack of biological persistence does NOT mean lack of toxicity, particularly for chemicals like PFAS that may have consistent daily exposures.

Traditional methods for measuring the body burden of PFAS—namely analyzing serum—are not as effective for shorter chain PFAS as for longer chain PFAS. Scientists are beginning to measure PFAS in urine,<sup>83</sup> in plasma, and in whole blood, as well as in serum.<sup>84</sup> These expanded biomonitoring techniques for sampling and analyses will further inform our understanding of exposures and risks. Using these techniques, many scientists are rightly focusing on measuring the total exposure to all PFAS as opposed to the past focus on one substance in isolation. This is important as it allows for understanding cumulative effects of PFAS mixtures as a class. Examining the person in the context of the measure of all the exposures they have experienced in their lifetime and how they relate to their health is in step with the latest science.

Approaching PFAS as a class for assessing exposure and biological impact is the most prudent approach to protect public health. Based upon their persistent nature, widespread exposure, and known toxicity, it begs the question: does the net value of PFAS production and use for modern-day convenience outweigh the likely risks to public health and associated healthcare costs? Thus, scientific and technology innovation is critical to enable a shift to safer alternatives, as appropriate.

Manufacturers have begun recently to produce and market AFFF devoid of any PFAS. Such fluorine-free AFFF is now being used at Heathrow Airport in London, United Kingdom and at major airports in Sweden. It will be important to evaluate these alternatives for potential health effects as well.

## **Federal Collaboration**

NIEHS and the NTP will continue to provide scientific leadership with respect to PFAS research. Communication and collaboration both within the Department of Health and Human Services, and across the Federal Government, about PFAS is intensifying. In February 2018, a Federal information exchange meeting about PFAS was held on the NIH campus in Bethesda, Maryland.<sup>85</sup> NIEHS was among other Federal agencies that participated at the PFAS National

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<sup>83</sup> Hartmann C, Rafflesberg W, Scharf S, Uhl M. Perfluoroalkylated Substances in Human Urine: Results of a Biomonitoring Pilot Study. *Biomonitoring* 2017; 4:1-10. DOI: [10.1515/bimo-2017-0001](https://doi.org/10.1515/bimo-2017-0001).

<sup>84</sup> Poothong S, Thomsen C, Padilla-Sanchez JA, Papadopoulou E, Haug LS. Distribution of Novel and Well-Known Poly- and Perfluoroalkyl Substances (PFASs) in Human Serum, Plasma, and Whole Blood. *Environ. Sci. Technol.* 2017 Nov 21; 51(22):13388-13396. DOI: [10.1021/acs.est.7b03299](https://doi.org/10.1021/acs.est.7b03299).

<sup>85</sup> Lenox K. Federal Agencies Exchange PFAS Updates. *NIEHS Environmental Factor*. 2018, Mar. Internet:



Leadership Summit hosted by EPA in May 2018.<sup>86</sup> Within the Department of Health and Human Services and primarily through NTP, NIEHS works closely with the FDA and the CDC on PFAS matters. Additionally, NIEHS is specifically being consulted by ATSDR on the design and conduct of the exposure assessments and health studies authorized by the National Defense Authorization Act for Fiscal Year 2018, as amended.<sup>87</sup>

## **Conclusion**

Thank you again for allowing me to share a scientific perspective on this important topic. In closing, I note that NIEHS is well-positioned to continue contributing essential scientific knowledge about this complex and large class of chemicals. This knowledge can help regulators make sound, science-based decisions and informs the medical and public health communities about the potential health effects associated with exposure to PFAS. I welcome your questions.

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<https://factor.niehs.nih.gov/2018/3/science-highlights/pfas/index.htm>.

<sup>86</sup> U.S. Environmental Protection Agency. EPA PFAS National Leadership Summit and Engagement. May 22-23, 2018. Internet: <https://www.epa.gov/pfas/pfas-national-leadership-summit-and-engagement>.

<sup>87</sup> Sec. 316 of the National Defense Authorization Act for Fiscal Year 2018. [Public Law 115-91](#). December 12, 2017.

**Appendix to Testimony of Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S.  
Director, National Institute of Environmental Health Sciences (NIEHS) and  
National Toxicology Program (NTP), National Institutes of Health (NIH)  
Senate Committee on Environment and Public Works Hearing – March 28, 2019**

**LIST OF CITATIONS TO PUBLICATIONS ABOUT  
PER- AND POLYFLUOROALKYL SUBSTANCES (PFAS)  
AUTHORED BY NIEHS SCIENTISTS AND GRANTEES  
(January 1, 2018—March 13, 2019)**

**NIEHS OFFICE OF THE DIRECTOR (OD) –**

Ritscher A, Z Wang, M Scheringer, JM Boucher, L Ahrens, U Berger, S Bintein, SK Bopp, D Borg, AM Buser, I Cousins, J DeWitt, T Fletcher, C Green, D Herzke, C Higgins, J Huang, H Hung, T Knepper, CS Lau, E Leinala, AB Lindstrom, J Liu, M Miller, K Ohno, N Perkola, Y Shi, L Smastuen Haug, X Trier, S Valsecchi, K van der Jagt and L Vierke  
**Zurich Statement on Future Actions on Per- and Polyfluoroalkyl Substances (PFASs)**  
[Journal Article]  
*Environmental Health Perspectives* (2018) v. 126 (8): pp. 84502  
Full-Text at: <http://dx.doi.org/10.1289/ehp4158>

**NIEHS DIVISION OF INTRAMURAL RESEARCH (DIR) –**

Impinen A, MP Longnecker, UC Nygaard, SJ London, KK Ferguson, LS Haug and B Granum  
**Maternal levels of perfluoroalkyl substances (PFASs) during pregnancy and childhood allergy and asthma related outcomes and infections in the Norwegian Mother and Child (MoBa) cohort** [Journal Article]  
*Environment International* (2019) v. 124 pp. 462-472  
Full-Text at: <http://dx.doi.org/10.1016/j.envint.2018.12.041>

Iszatt N, S Janssen, V Lenters, C Dahl, H Stigum, R Knight, S Mandal, S Peddada, A Gonzalez, T Midtvedt and M Eggesbo  
**Environmental toxicants in breast milk of Norwegian mothers and gut bacteria composition and metabolites in their infants at 1 month** [Journal Article]  
*Microbiome* (2019) v. 7 (1): pp. 34  
Full-Text at: <http://dx.doi.org/10.1186/s40168-019-0645-2>

Rosen EM, AL Brantsaeter, R Carroll, L Haug, AB Singer, S Zhao and KK Ferguson  
**Maternal Plasma Concentrations of Per- and polyfluoroalkyl Substances and Breastfeeding Duration in the Norwegian Mother and Child Cohort** [Journal Article]  
*Environmental Epidemiology* (2018) v. 2 (3): e027  
Full-Text at: <http://dx.doi.org/10.1097/ee9.0000000000000027>

Rush EL, AB Singer, MP Longnecker, LS Haug, A Sabaredzovic, E Symanski and KW Whitworth

**Oral contraceptive use as a determinant of plasma concentrations of perfluoroalkyl substances among women in the Norwegian Mother and Child Cohort (MoBa) study** [Journal Article]

*Environment International* (2018) v. 112 pp. 156-164

Full-Text at: <http://dx.doi.org/10.1016/j.envint.2017.12.015>

Singer AB, KW Whitworth, LS Haug, A Sabaredzovic, A Impinen, E Papadopoulou and MP Longnecker

**Menstrual cycle characteristics as determinants of plasma concentrations of perfluoroalkyl substances (PFASs) in the Norwegian Mother and Child Cohort (MoBa study)** [Journal Article]

*Environmental Research* (2018) v. 166 pp. 78-85

Full-Text at: <http://dx.doi.org/10.1016/j.envres.2018.05.019>

#### **NIEHS NATIONAL TOXICOLOGY PROGRAM (NTP) DIVISION –**

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