## DEPARTMENT OF HEALTH AND HUMAN SERVICES

# NATIONAL INSTITUTES OF HEALTH

### NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

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Testimonybefore the Senate Committee on Homeland Security and Goverratheffairs Subcommittee on Federal Spending Oversight and Emergency Management

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systems*in silico* approaches, and high throughput toxicological screenieg; annot ethically conductprospectivemechanistic studies in humans

The most conclusive human health research isolates a single variable to understand the cause and effect of that variable, whether it be a dragnicroorganismor a mutated gene. With possibly toxic chemicals, we arlargely limited to natural history and population as studies that attempt to find connection between populations exposed an earland the ffects in the real world. ) RUWKDWUHDVRQ \RXZLOOVLKREE attain Fred the ffects of the real world.

The research conducted to date reveals associations between human PFAS exposures and specific adverse human health outcomes include otential effects on

bioaccumulate, leading to concentrations in animalsatives significantly higher than the surrounding environment, and they can enter the human food chain.

Decreased Immune System Function As early as 1978, scientists observed immunotoxicity in non were found for PFOA, PFOS, PFHxS, PFDeA, and PFUA, but not for PPNAnimal studies are consistent with the human epidemiologuidises of cancer endpoints.

### Child Development

PFOA and PFOS aused evelopmental toxity in animals<sup>23,24,25</sup> Human epidemiology studies also show associations between mePFAS and developmental effects Onehuman study found that PFAS exposure during pregnancy was associated **dettreased** in the weight and head circumference only **in**ales<sup>27</sup> Similar decreases in birth weight have been reported in rodents for over a decade. Recent findings from NIFs upported epidemiological studies of a cohort of mothers and babies showed that prenatal exposure to PFOS is associated with cognitive effects and becreased ability to regulate behavior in schage children. However, no similar association was observed this study for PFOA exposure.

A review of the epidemiological literature by an NIE-HB ded scientist summarized findings from several prospetive cohorts on the relationship between premetpbsure to certain FAS and neurodevelopmental and neurobehavioral outcomforsexample, cognitive abilities, psychomotor development, attentide ficit hyperactivity disorder, and cerebral pal So far, the available body of evidence is inconsistent with respect to the scientist summarized for which compounds may have adverse effectisming of potential windows of vulnerability. Additional studies are needed to resolve these questions.

#### Endocrine Disruption

Studies suggest theomePFAS may interfere with healthy hormonal function in the body endocrine system on trol

development Studies suggest that earline exposure to somePFAS may contribute the development of metabolic diseases, including obesity and type 2 diabetes, which are major public health problems Although further confirmation is required, the findings fromestudy suggest that problems to some FAS during pregnancy may influence lipid metabolism and glucose tolerance A study of pregnant women in Cincinnati found that those with higher prenatal PFAS levels had children with higher body fat levels at age<sup>2</sup> eightinding reinforced by other epideorio bigical studie<sup>3</sup>, <sup>34</sup> and similar effects on excessive body weight gain reported for experimental animalist appears that some PFAS may also affect body weight later in life. Scientists at the Harvard School of Public Health have found that vitual higher blood levels of ome PFAS have lower resting metabolic rates, meaning they burn fewer calories while resting, which makes it difficult for them to maintain weight<sup>36</sup> bigs fects on weight gain have been seen in numerous animal st<sup>37</sup> dfe<sup>38</sup>, supporting this association in humans. this particularly concerning the there is a metabolism and grow<sup>411.42</sup>

<sup>&</sup>lt;sup>31</sup> Matilla-Santander N, Valvi D, Lope Espinosa MJ, Manzan Salgado CB, Ballester F, Ibarluzea J, Salvarina L, Schettgen T, Guxens M, Sunyer J, Vrijheid M. Exposure to Perfluoroalkyl Substances and Metabolic Outcomes in Pregnant Women: Evidence from Beanish INMA Birth Cohorts *Environ Health Perspect*. 2017 Nov

<sup>13;125(11):117004.</sup> DO10.1289/EHP1062

<sup>&</sup>lt;sup>32</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 *Studyty (Silver Spring)*. 2016 Jan;24(1):2347. DOI:10.1002/oby.21258

<sup>&</sup>lt;sup>33</sup> Mora AM, Oken E, Rifas Shiman SL, Webster TF, Gillman MVC, alafat AM, Ye X, Sagiv SK. Prenatal Exposure to Perfluoroalkyl Substances and Adiposity in Early ane Ovlited hood. *Environ Health Perspect*. 2017 Mar;125(3):467473. DOI:10.1289/EHP246

<sup>&</sup>lt;sup>34</sup> Karlsen M, Grandjean P, Weihe P, Steuerwald U, Oulhote Y, Valvi D. **Eferle**xposures to persistent organic pollutants in relation to overweight in preschool child *merprod Toxicol*. 2017 Mar;68:145153. DOI:10.1016/j.reprotox.2016.08.002

<sup>&</sup>lt;sup>35</sup> Hines EP, White SS, Stanko JP, Gib Bisurnoy EA, Lau C, Fenton SE. Phenotypic dichotomy following developmental exposure to perfluorooctanoic acid (PFOA) in female 600ce: Low doses induce elevated um leptin and insulin, and overweight in milde. *Mol Cell Endocrinol*. 2009 May 25;304(-2):97-105. DOI: 10.1016/j.mce.2009.02.021

<sup>&</sup>lt;sup>36</sup> Liu G, Dhana K, Furtado JD, et al. Perfluoroalkyl subsesmend changes in body weight and resting metabolic rate in response to weights diets: A prospective study. Basu S, *PetchS Medicine*. 2018;15(2):e1002502. DOI: <u>10.1371/journal.pmed.10025</u>02

<sup>&</sup>lt;sup>37</sup> Grün F, Blumberg B. Endocrine disrupters as obesog**ens***Cell Endocrinol*. 2009 May 25;304(**2**):19-29. DOI:<u>10.1016/j.mce.2009.02.0</u>18

<sup>&</sup>lt;sup>38</sup> Shi Z, Zhang H, Ding L, Feng Y, Xu M, Dai J. The eest of perfluorododecanonic acid on endocrine status, sex hormones and expression of steroido 1 456.79in BT /F1 9.96 Tf .00912 0 612 792 re ] TJ Eta Gc0 1 72.021 Gc0 1 72.02

Fertility is another outcome related to endocrine effectiviterature review of recent human epidemiologic evidence on the association between expossionentePFAS and measures of human fertility show the potential for effects formale fecundability (i.e., the probability of conception)<sup>4.3</sup> In addition, several recent studies have shown an association between women with higher PFAS exposured the ength of time they are able to nurse their child after birth although not at all levels of exposured breastfeedinguring and after pregnancy in mice.

### NIEHS

potential toxicity, how it is stored in the body, and how long it remains in the environt the Initial results from nearly 200 homes show detectable levels of GenX in treated tap water from the Cape Fear River but none above 140 parts per trillion, the **cNoreth**tCarolinapublic health goal for GenX in drinking wateMany other PFAS were alsoceasured in treated Cape Fear River tap water. GenX was not detected to the tap water of homes whose groundwater was treated with granular activated carbon filtratioAdditional analysis, including testing of blood and urine samples from study participants, is ongoing. NTP is also studying how GeneX move through the body and whether it is toxic to the placenta, immune system, liver, and other tissues.

## NTP REACT Program

The NTP Responsive Evaluation and Assessment of Chemical Toxicity, or REAGGT am is studying subclasses of PFAS, due to potential similarities in chemical properties and toxicity within subclasses. Scientists will be able to compare one REFAS other, determine the relationship between chain length anching and toxicity, and work toward understanding a common basis for toxicity.

REACT uses a combination of method sirst, the project analyzes the chemical structure of PFAS compounds the 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 is computed based site is known as *in silico* screening. Based on *silico* results, chemicals are prioritized for further laboratory testing with cells, known as *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 conducted through the automated Toxicology in the 21st Century (Tox21) Program a Federal collaboration amortige NIH, the U.S. Environmental Protection Agency (EPA), and the S. Food and Drug Administration (FDAS) The *in vitro* data are then examined to prioritize select chemicals for toxicity testing in animals, known as studies, so the data can be considered all together. REACT is a collaborative program Plans to test over 100 individual PFAS ross the FAS class. Both NTP and EPA are generating chemical libraries to consolidate and share what is known about individual chemicals.

### **Current Challenges**

Real-world human exposures to PFAS volve complex mixtures, not individual chemicals his fact complicates both the science of exposure and the assessimeat horisks.<sup>57</sup> Currently, analytical techniques are limited for determining which specific PFAS are **need** tian a given

<sup>&</sup>lt;sup>54</sup>NIH Grant No. R21ES029353. Assessing Impact of Drinking Water Exposure to GenX (Hexafluoropropylene Oxide Dimer Acid) in the Cape Fereview Basin, North Carolina. Hoppin, Jane. North Carolina State University, Raleigh. Awarded on October 31, 2017/IH RePORTER Link

<sup>55</sup> Researchers - 56(s) 30(/) - 2[((R-)3)(-60) 03(99)B(x)(6R))3 Cb)78itt + bd0 1ided on October 3e0v4143.06 Tm 0 g 0 G 4(mi)-3(c)4(a)4(lul

complex mixture. Furtherotxicological information on these mbined

Leadership Summit hosted by ERAMay 2018<sup>61</sup> Within the Department of Health and Human Services and primarily through NTP, NIEHS works closely whith FDA and the Centers for Disease Control and Preventic D(C) on PFAS matters. Additionally, NIEHS is specifically being consulted by ATSDR on the execution of the posure assessments and the summarial through authorized by the National Defense Autization Actfor Fiscal Yea 2018 as amended

### Conclusion

Thank you again for allowing me to share a scientific perspective on this important topic. In closing, I note that NIEHS is wellositioned to continue contributiregssentialscientific knowledge about this complex and large class of chemicals. This knowledge can help regulators make sound, sciendersed decisions and informs the medical and public health communities about the potential health effects associated with exposs PEAS. I welcome your questions.

<sup>&</sup>lt;sup>61</sup> EPA PFAS National Leadership Summit and Engagement. Ma2322018. Internet: https://www.epa.g