NIEHS PFAS Research: Enabling Evidence-Based Strategies

Brian R. Berridge, D.V.M., Ph.D., DACVP
Scientific Director
Division of the National Toxicology Program
National Institute of Environmental Health Sciences (NIEHS)

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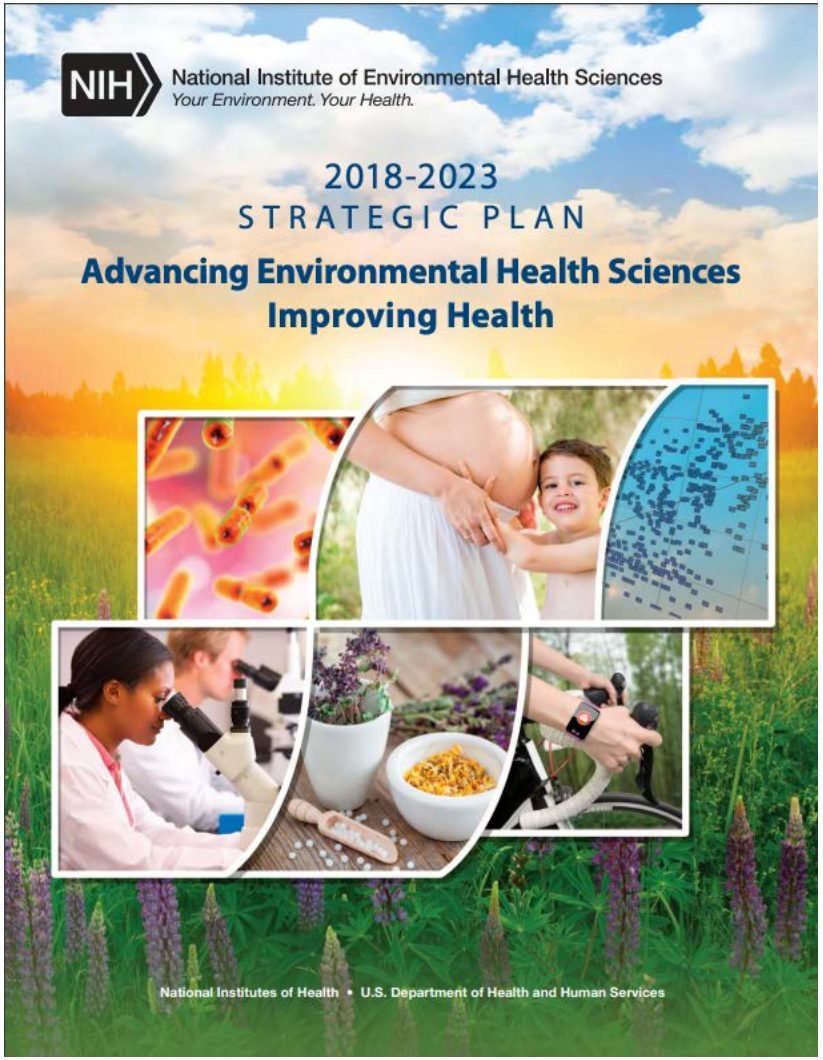
National Institute of Environmental Health Sciences



Mission Statement

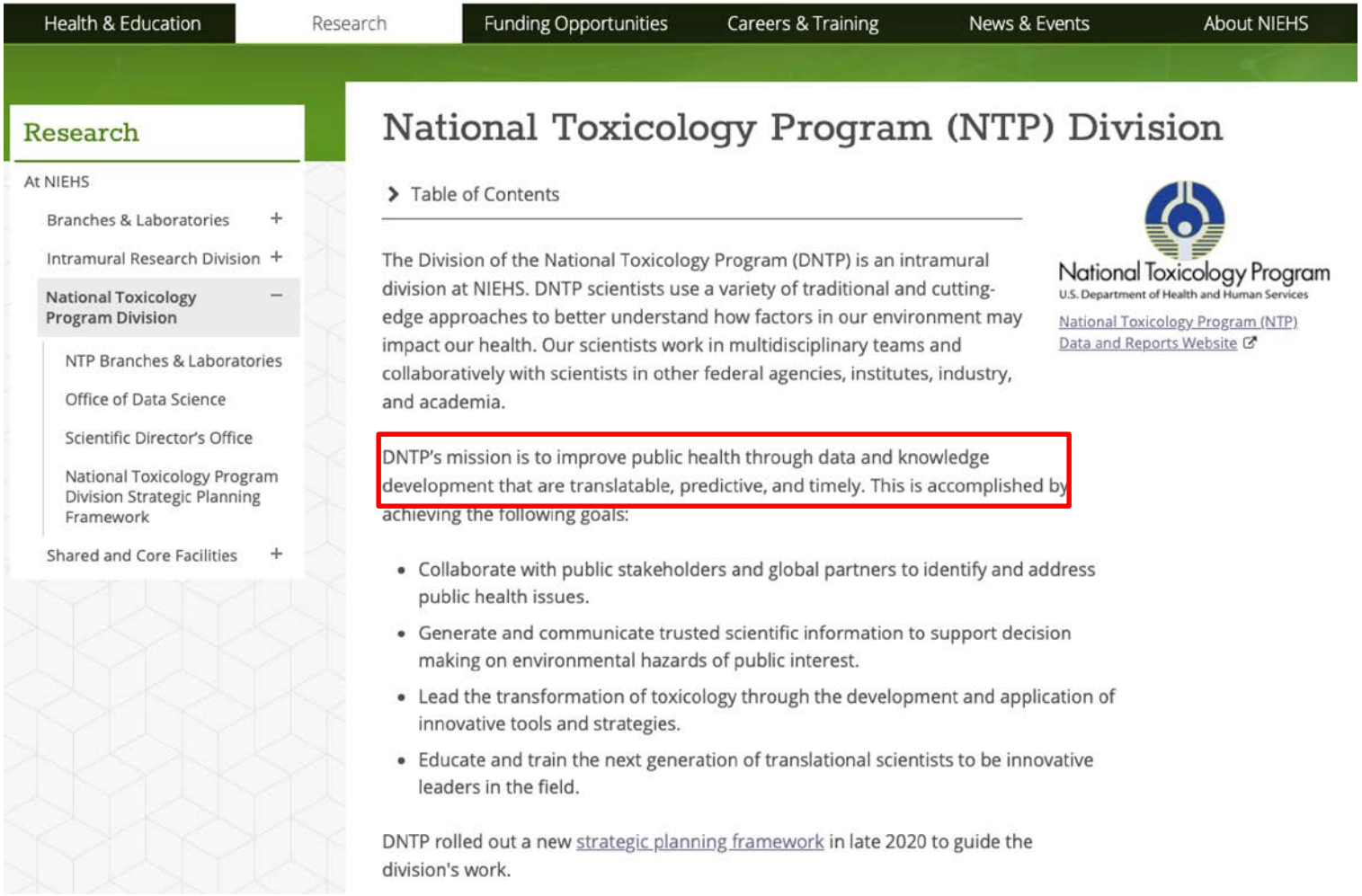
The mission of the National Institute of Environmental Health Sciences is to discover how the environment affects people in order to promote healthier lives.

Vision Statement

The vision of the National Institute of Environmental Health Sciences is to provide global leadership for innovative research that improves public health by preventing disease and disability.

- **Advancing Environmental Health Sciences**
- **Promoting Translation – Data to Knowledge to Action**
- **Enhancing EHS Through Stewardship and Support**

NIEHS National Toxicology Program Division

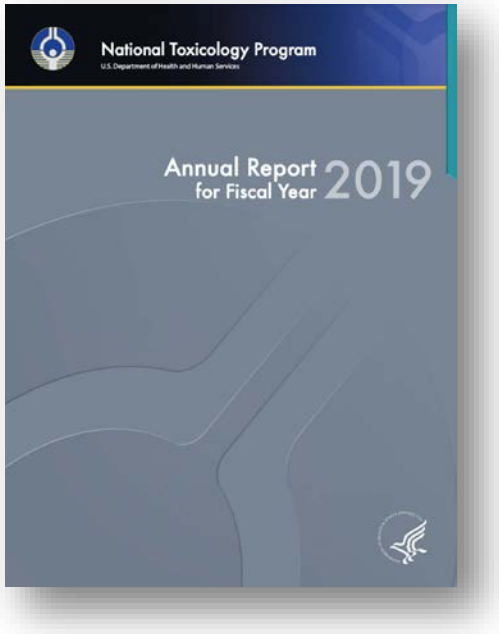


US Department of Health and Human Services (DHHS)
Asst. Secretary of Health

- NIH
  - NIEHS
    - DNTP
- CDC
  - NIOSH
- FDA
  - NCTR

National Toxicology Program
U.S. Department of Health and Human Services

http://ntp.niehs.nih.gov



- Hazard identification and characterization
- Developing novel tools and capabilities
- Advancing scientific knowledge

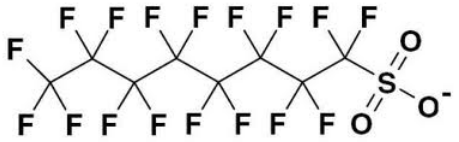
What are Per- and Polyfluoroalkyl Substances (PFAS)?

- **Total number of PFAS**

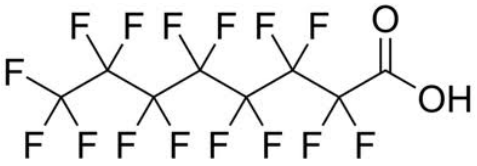
  >5,000 chemicals

  – Includes products, impurities and degradants

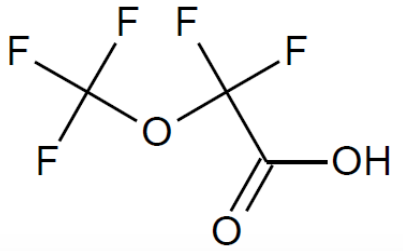
- Resistant to grease, water & oil
- Persistent and bio-accumulative
- Lots of potential health effects



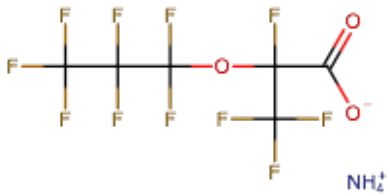
PFOS



PFOA



PFMOAA



GenX

Extramural Research

National Institute of Environmental Health Sciences
Your Environment. Your Health.

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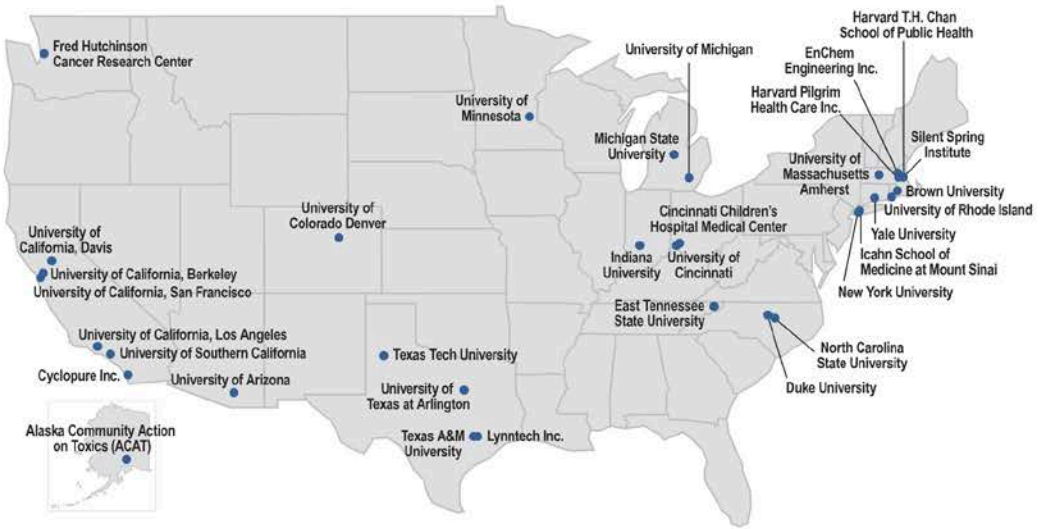
Research

- Funded by NIEHS Grants
  - Environmental Exposure Research
    - Per- and Polyfluoroalkyl Substances (PFAS)
      - Highlighted Research +
      - NIEHS-Supported Researchers Focusing on PFAS
      - Published Studies Funded by Grants
      - Related Resources
      - Upcoming Events

NIEHS-Supported Researchers Focusing on PFAS

NIEHS supports more than 40 research groups across the country to better understand the health effects of PFAS.

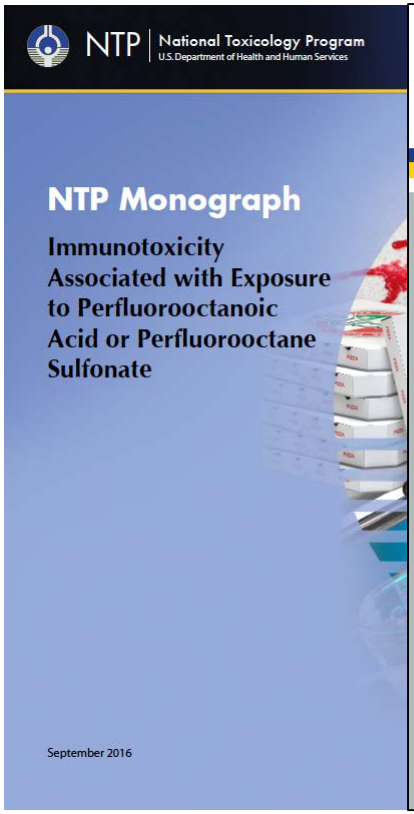


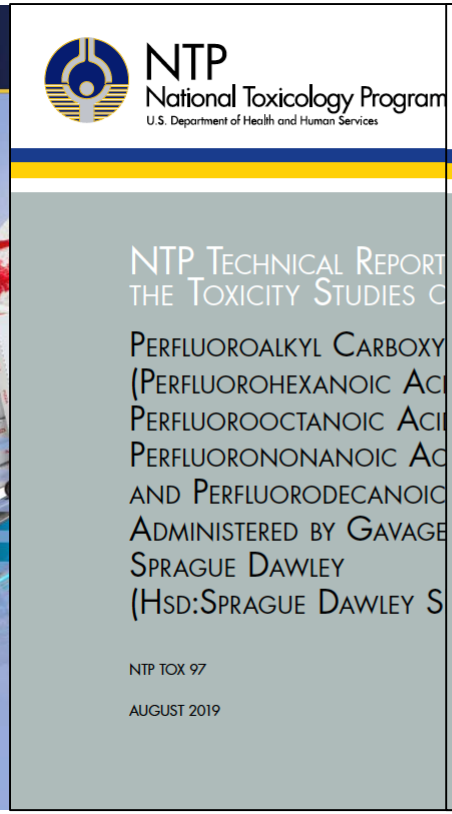
NIEHS PFAS Grants Portfolio

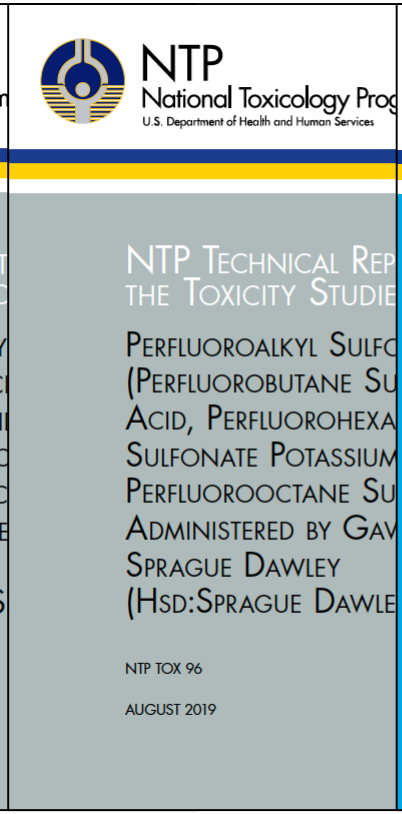
— **Awards via various NIH funding mechanisms**, including:

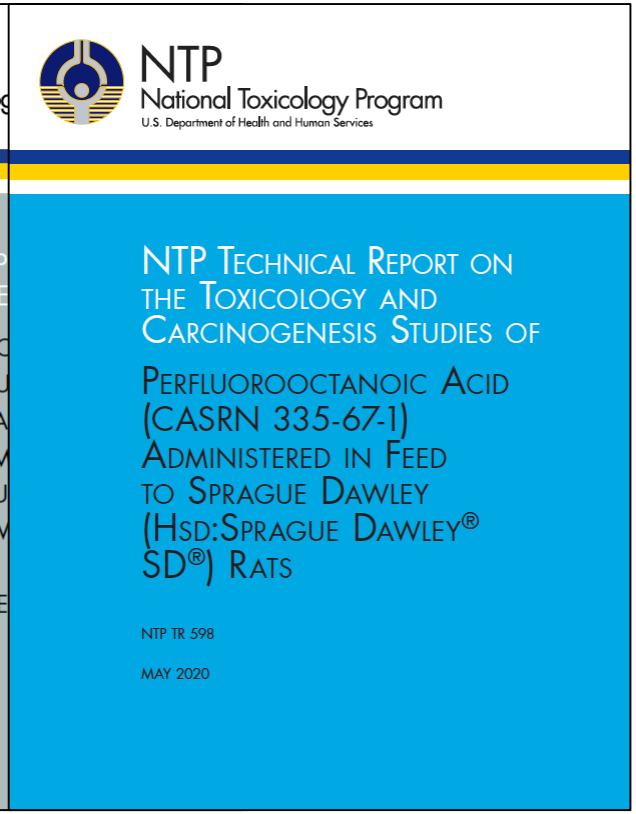
- Investigator-initiated basic research
- Time-sensitive awards
- SBIR (Small Business Innovation Research) program grants
- NIEHS/EPA Children's Environmental Health and Disease Prevention Research Centers
- Breast Cancer and The Environment Research Program
- Superfund Research Centers
- Conference support
- Environmental influences on Child Health Outcomes (ECHO) program awards

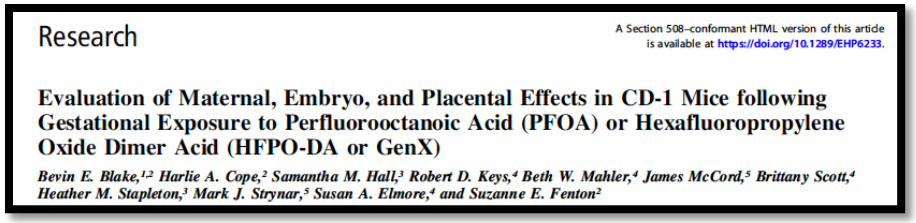
DNTP Research Products







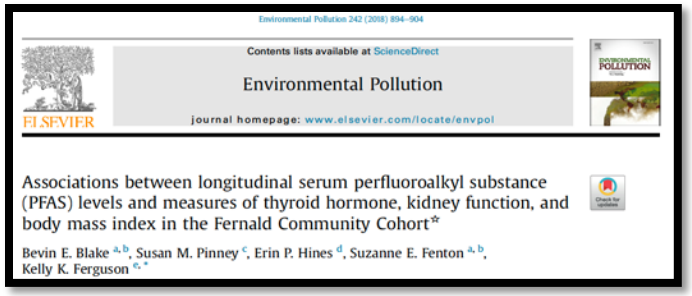



Research

A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP6233.

Evaluation of Maternal, Embryo, and Placental Effects in CD-1 Mice following Gestational Exposure to Perfluorooctanoic Acid (PFOA) or Hexafluoropropylene Oxide Dimer Acid (HFPO-DA or GenX)

Bevin E. Blake,[1,2] Harlie A. Cope,[2] Samantha M. Hall,[3] Robert D. Keys,[4] Beth W. Mahler,[4] James McCord,[5] Brittany Scott,[4] Heather M. Stapleton,[3] Mark J. Strynar,[5] Susan A. Elmore,[4] and Suzanne E. Fenton[2]



Associations between longitudinal serum perfluoroalkyl substance (PFAS) levels and measures of thyroid hormone, kidney function, and body mass index in the Fernald Community Cohort☆

Bevin E. Blake [a, b], Susan M. Pinney [c], Erin P. Hines [d], Suzanne E. Fenton [a, b], Kelly K. Ferguson [c, *]

Current DNTP PFAS Research

- Systematic literature review
  - Immunotoxicity of select PFAS
- Short duration in vivo transcriptomics
  - Predictive toxicology
- REACT Program-
  - Responsive Evaluation and Assessment of Chemical Toxicity
  - Read across capabilities
- AFFF assessments
  - In vitro and in vivo characterization of hazard

Key Messages

- The role of NIEHS and NTP is to characterize possible health effects of PFAS chemicals
  - Accomplished through extramurally-funded academic research, intramural research, and NTP experimental investigation
- Human and animal evidence suggest that PFAS may have health effects in people
  - Potential health effects are numerous including effects in the liver, kidney, thyroid, pancreas, immune system, on metabolism, and on early life development
  - Most data are for older generation PFAS (i.e., PFOA and PFOS)
- We would like to understand better the human relevance of the health effects that have been described
- We would like to understand better the most important 'human' concerns to help in prioritizing our research efforts

Expectations

116TH CONGRESS 2d Session | HOUSE OF REPRESENTATIVES | REPORT 116–617

WILLIAM M. (MAC) THORNBERRY
NATIONAL DEFENSE AUTHORIZATION ACT
FOR FISCAL YEAR 2021

CONFERENCE REPORT

TO ACCOMPANY

H.R. 6395

DECEMBER 3, 2020.—Ordered to be printed

U.S. GOVERNMENT PUBLISHING OFFICE
42–147 WASHINGTON : 2020

SEC. 332. INTERAGENCY BODY ON RESEARCH RELATED TO PER- AND POLYFLUOROALKYL SUBSTANCES.

(a) ESTABLISHMENT.—The Director of the Office of Science and Technology Policy, acting through the National Science and Technology Council, shall establish, or designate, an interagency working group to coordinate Federal activities related to PFAS research and development.

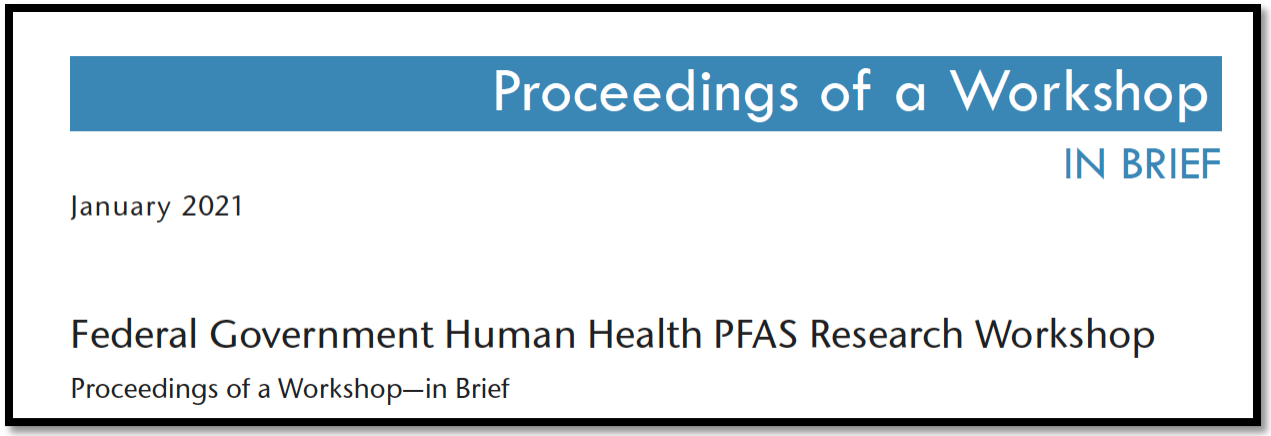
(b) AGENCY PARTICIPATION.—The interagency working group shall include a representative of each of—

(1) the Environmental Protection Agency;
(2) the National Institute of Environmental Health Sciences;
(3) the Agency for Toxic Substances and Disease Registry;
(4) the National Science Foundation;
(5) the Department of Defense;
(6) the National Institutes of Health;
(7) the National Institute of Standards and Technology;
(8) the National Oceanic and Atmospheric Administration;
(9) the Department of the Interior;
(10) the Department of Transportation;
(11) the Department of Homeland Security;
(12) the National Aeronautics and Space Administration;
(13) the National Toxicology Program;
(14) the Department of Agriculture;
(15) the Geological Survey;
(16) the Department of Commerce;
(17) the Department of Energy;
(18) the Office of Information and Regulatory Affairs;
(19) the Office of Management and Budget; and
(20) any such other Federal department or agency as the Director of the Office of Science and Technology Policy considers appropriate.

(C) identifies scientific and technological challenges that must be addressed to understand and to significantly reduce the environmental and human health impacts of PFAS and to identify cost-effective—

(i) alternatives to PFAS that are designed to be safer and more environmentally friendly;

Research Needs


Proceedings of a Workshop

IN BRIEF

January 2021

Federal Government Human Health PFAS Research Workshop

Proceedings of a Workshop—in Brief

https://www.nap.edu/catalog/25856/understanding-controlling-and-preventing-exposure-to-pfas-proceedings-of-a

- Information on mechanism of action, dose-response relationships, and mixtures
- Pharmacokinetic data- human half-lives, hepatic clearance, metabolic susceptibility, renal absorption, effect of population variability
- Better understanding of mechanisms of immune effects
- Biologic plausibility and mechanisms of action through which PFAS can influence cancer development
- Better understanding of understudied reproductive and developmental effects
- Determining how innovative studies such as intervention-based approaches may provide more complete information on health outcomes

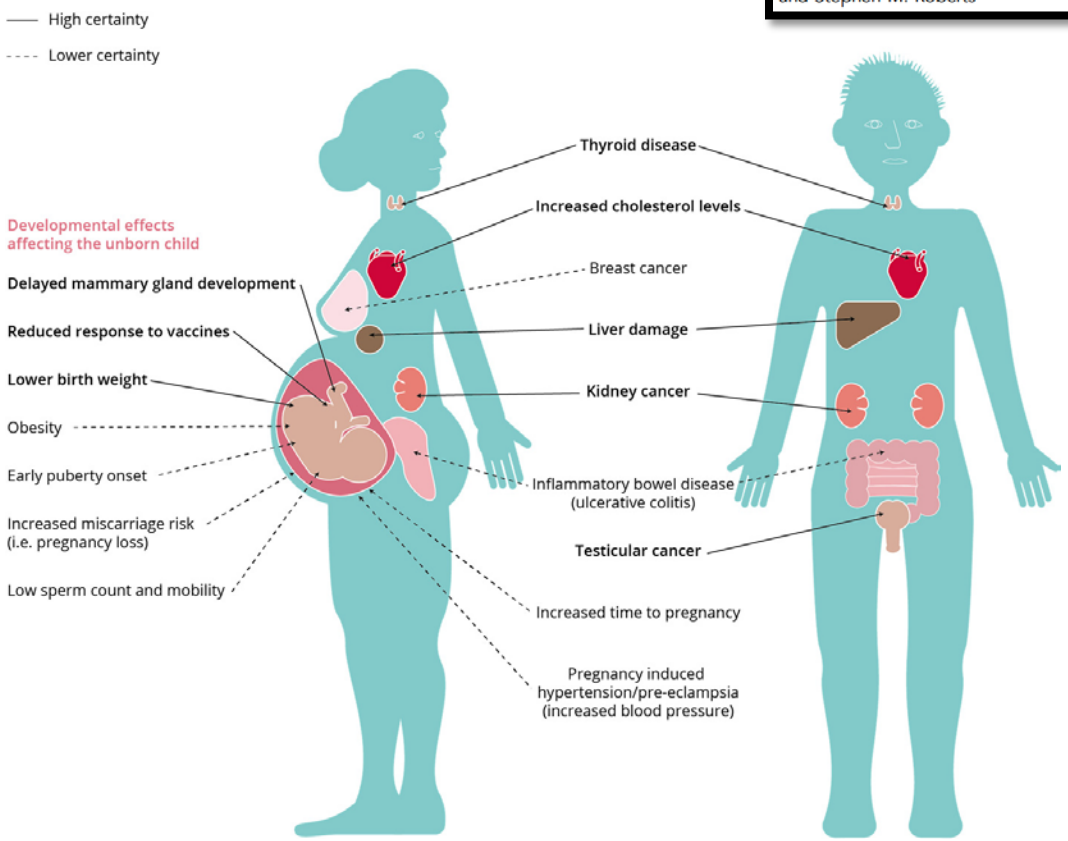
Health Effects

Environmental Toxicology and Chemistry—Volume 00, Number 00—pp. 1–25, 2020
Received: 20 July 2020 | Revised: 29 August 2020 | Accepted: 20 September 2020 1

Critical Review

Per- and Polyfluoroalkyl Substance Toxicity and Human Health Review: Current State of Knowledge and Strategies for Informing Future Research

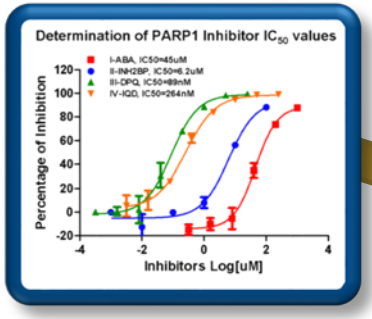
Suzanne E. Fenton,[a] Alan Ducatman,[b] Alan Boobis,[c] Jamie C. DeWitt,[d] Christopher Lau,[e] Carla Ng,[f] James S. Smith,[g] and Stephen M. Roberts[h,*]



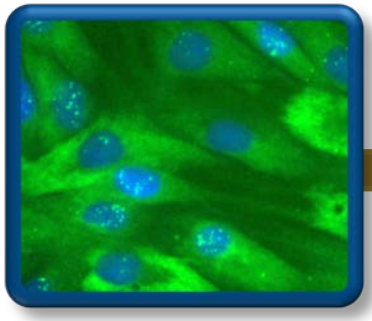
- Many putative human health effects
- Varying levels of evidence to support
- Difficult to prioritize most important threats based on varying exposures

DNTP Research Capabilities

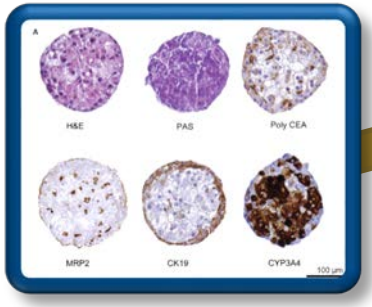
Bioactivity Screening

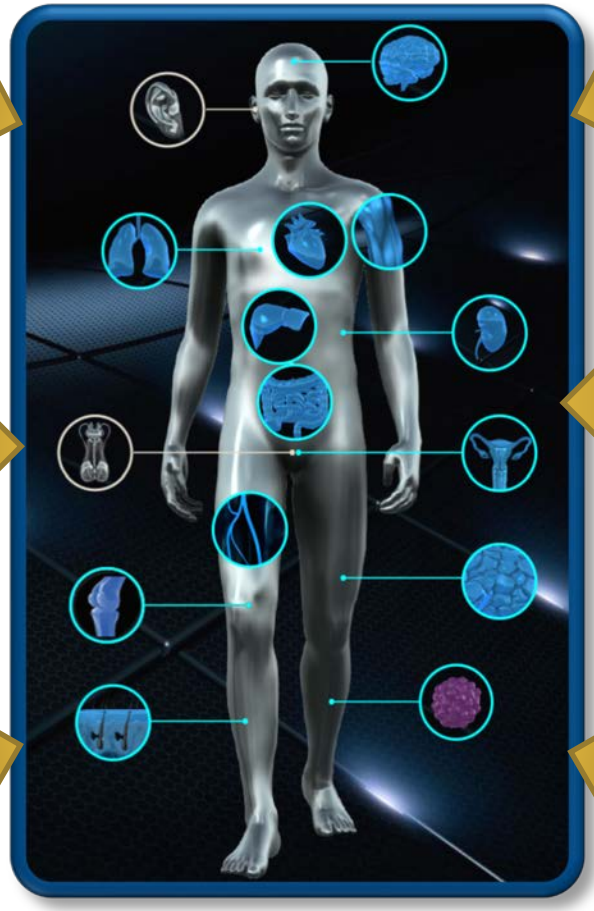


Simple In Vitro Studies



Complex In Vitro Systems





Computational Analysis

Integrated Health Assessments

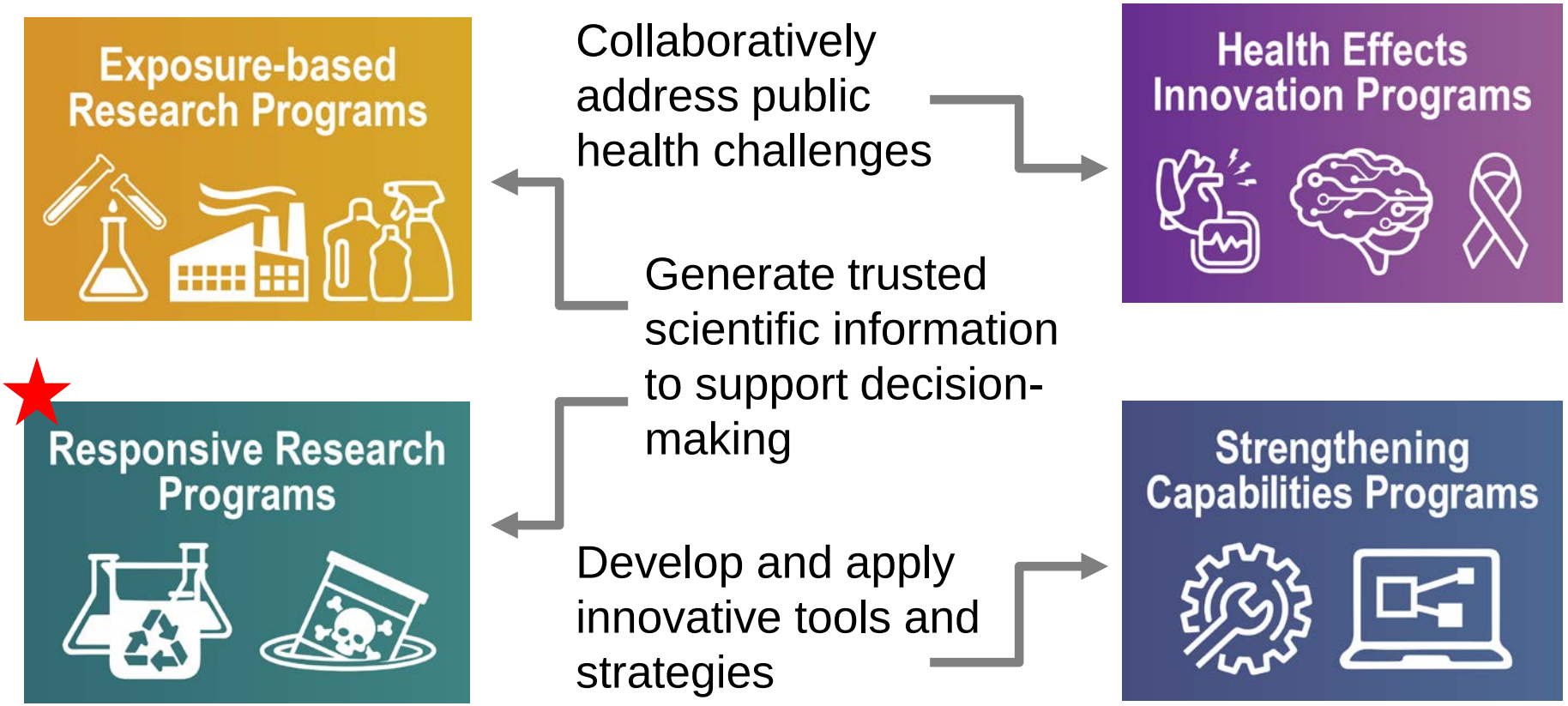
Animal Studies

https://ncats.nih.gov/tissuechip/chip

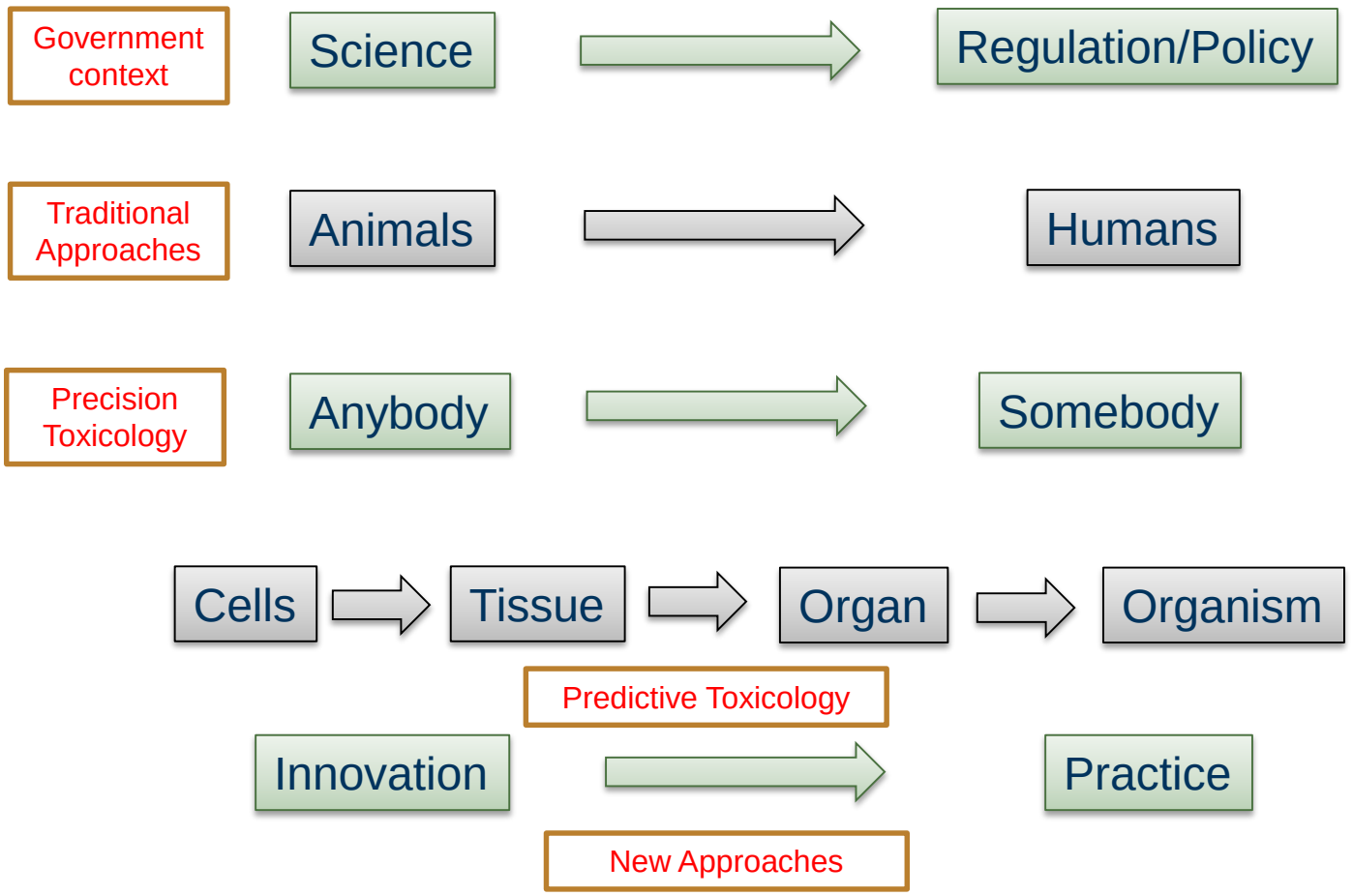
DNTP Research Prioritization

- Nominations
  - External, internal
  - Government, non-government
- Exposure-based concerns
- Lack of data
- Human evidence
- Animal/experimental evidence
- Leveraging our non-regulatory and independent role

DNTP Strategic Areas of Focus



‘Translation’ the DNTP way



PFAS Challenges

PFAS Research Prioritization Challenges

- Which PFAS?
  - Individual agents
  - Mixtures
  - Class-based approaches
  - Exposure vs. potency
- Which health effects?
- Which people?
  - Life stage
  - Co-morbidities
  - Genetic susceptibility
- What kind of data?
  - Usual in vivo guideline studies
  - Relevance of animal systems?
    - PPAR alpha bioactivity
  - HTP bioactivity screening
  - MTP cell/tissue-based characterization
- Build tools/capabilities vs. generate data?

Opportunity to help us

Project Title: Guidance on PFAS Testing and Health Outcomes

Assess the strength of evidence for the spectrum of putative health effects suggested by human studies (including immune response, lipid metabolism, kidney function, thyroid disease, liver disease, glycemic parameters and diabetes, cancer, and fetal and child development) to establish a basis for prioritized clinical surveillance or monitoring of PFAS health effects. This assessment should characterize the likelihood of those health effects occurring (qualitative probability) given real world human exposures and identify the human populations at most risk (consider life stage, health status, exposure level). Data/evidence gaps that contribute to uncertainty about health effects of most concern should be annotated.

Evidence gaps = Research Priorities

Thank you in advance for your effort!

Questions?