Sunderland Lab members collecting shellfish from Quashnet River. Photo: Sunderland Lab.

STEEP Progress on the PFAS Challenge: Protecting Human and Environmental Health

2021 Progress

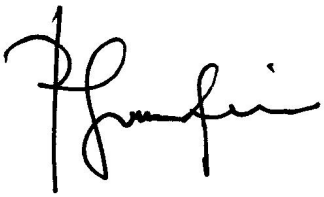
STEEP
Sources, Transport, Exposure & Effects of PFASs
UNIVERSITY OF RHODE ISLAND SUPERFUND RESEARCH PROGRAM

University of Rhode Island

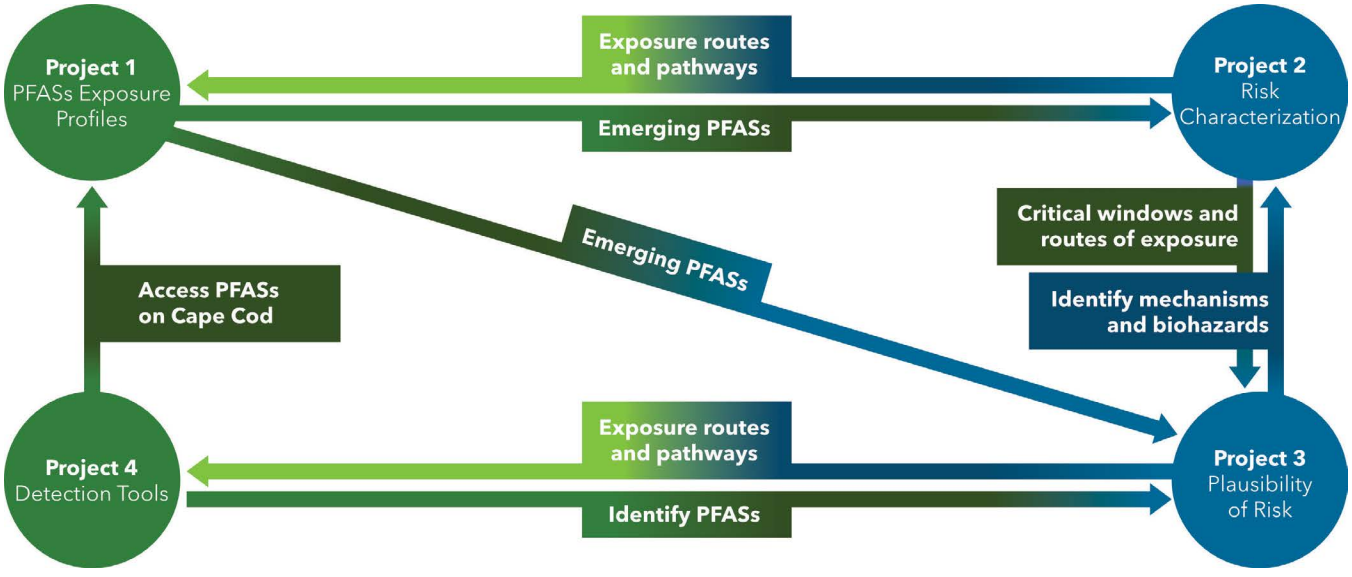
I have been working for over 20 years on legacy and emerging contaminants with particular focus on the coastal marine environment. From dioxins to PCBs, I have seen the damage that human-produced chemicals have wrought on human and environmental health; however, PFAS present a whole new level of challenges as they are extremely persistent and ubiquitous in the environment. STEEP will continue to work with its stakeholders to ensure that the best available science is used to protect people from undue PFAS exposure, though COVID-19 made progress more difficult. Stay safe!

For many years I have dedicated my medical research to environmental epidemiology. My main emphasis is on the adverse health effects of environmental chemicals—in particular the long-term implications of early-life exposures. PFAS can negatively affect the maturation of important organ functions, and a major concern is the insidious threat of PFAS exposure to the immune system. In a time with widespread COVID-19 infections, a fully functional immune system is crucial. Through the support of NIEHS, STEEP supports our highest aspirations in addressing and preventing adverse health impacts from the PFAS.

Lead **Rainer Lohmann, PhD**
Graduate School of Oceanography
University of Rhode Island



Co-lead **Philippe Grandjean, MD DMSc**
Harvard T.H. Chan School of Public Health,
Department of Environmental Health



Director Lohmann and co-Director Grandjean combine complementary expertise in environmental and epidemiological science. They brought together a team of individuals that function as an effective and integrated interdisciplinary team. This includes researchers from the University of Rhode Island Graduate School of Oceanography, the Coastal Institute, and Colleges of Pharmacy, Engineering, and the Environment and Life Sciences; Harvard T.H. Chan School of Public Health, Department of Environmental Health; and the Silent Spring Institute.

STEEP Overview

Per- and polyfluorinated alkyl substances (PFAS) are extremely resistant to environmental degradation and are found in humans and the environment around the world. Due to the persistence, adverse effects can build over time.

The most notable PFAS include perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS). In the U.S., there are industrial PFAS production and manufacturing sites, and over 600 fire/crash training sites nationwide where PFAS-containing aqueous film-forming foams have most likely contaminated groundwater, soil and sediments. Additional human exposure results from widespread use of PFAS in consumer products, e.g., stain-resistant furnishings and carpets, grease-proof food packaging and wrappers. Production and use of PFOS and PFOA have declined in the U.S. since the early 2000s following a voluntary phase-out by 3M, along with subsequent stewardship plans by U.S. EPA, action involving several major U.S. producers and international agreements. Industrial production in the U.S. shifted away from PFOA and PFOS as the public was provided evidence of their adverse human health impacts. As production decreased in the U.S., new fluorinated compounds have been and continue to be developed to meet anticipated market demands. As a result, environmental contamination and human exposure continues.

Despite widespread PFAS use since the 1950s, there is still incomplete documentation about their environmental and public health impacts, thus these contaminants are considered emerging. STEEP is committed to assessing environmental and human health concerns to inform development of appropriate benchmark dose levels for PFAS. Moreover, STEEP will disseminate these research results to a variety of stakeholders as well as train the next generation of scientists essential to the management of these highly stable and ubiquitous compounds. Over the last few years, there has been a burgeoning awareness of the ubiquity of PFAS and its transport through consumer goods into the food web. From Maine dairy farms to the global registry of thousands of PFAS, presence of these “forever chemicals” in humans and ecosystems is of growing concern and in urgent need of widespread attention.

RESEARCH PROJECTS OVERVIEW

STEEP Research Projects aim to better understand the pathways of PFAS contamination from entry into the environment through groundwater contamination, dispersal through the food web, and distribution to vulnerable human populations during early development, in part through breast milk. In addition, STEEP supports the development and deployment of in situ passive sampling techniques for PFAS and their precursors in water and air. STEEP is thereby addressing limitations in the current understanding of human exposure to PFAS by combining targeted human exposure assessment with chemometric approaches to characterize existing PFAS sources.

CORE OBJECTIVES OVERVIEW

To ensure a legacy of scientific awareness, dissemination of broadly accessible research findings, and practical application by affected communities, STEEP Cores serve to prepare the next generation of interdisciplinary emerging contaminant researchers, translate scientific findings generated by STEEP projects for internal and external stakeholders, and engage Cape Cod communities on the front lines of PFAS exposure through contaminated drinking water.

Communities

Puffins at Mykines, Faroe Islands. Photo: Stefan Wisselink, https://www.flickr.com/people/135727714@N06.

STEEP is focused on two study sites, one on Cape Cod and the other in the Faroe Islands. Barnstable County, MA, is STEEP's primary site for community engagement activities. STEEP partner Silent Spring Institute has conducted community-engaged research and activities focused on water quality and public health—with a particular emphasis on PFAS—on Cape Cod for more than 20 years.

The Faroe Islands are STEEP's epidemiological research site, where for decades co-director Grandjean, in partnership with Pál Weihe, MD (Adjunct Professor, University of the Faroe Islands; Head, Department of Occupational Medicine and Public Health), has studied the impact of early-life exposures to persistent chemicals on health and development. The focus on highly vulnerable early development enriches STEEP's understanding of the adverse health impacts of PFAS.

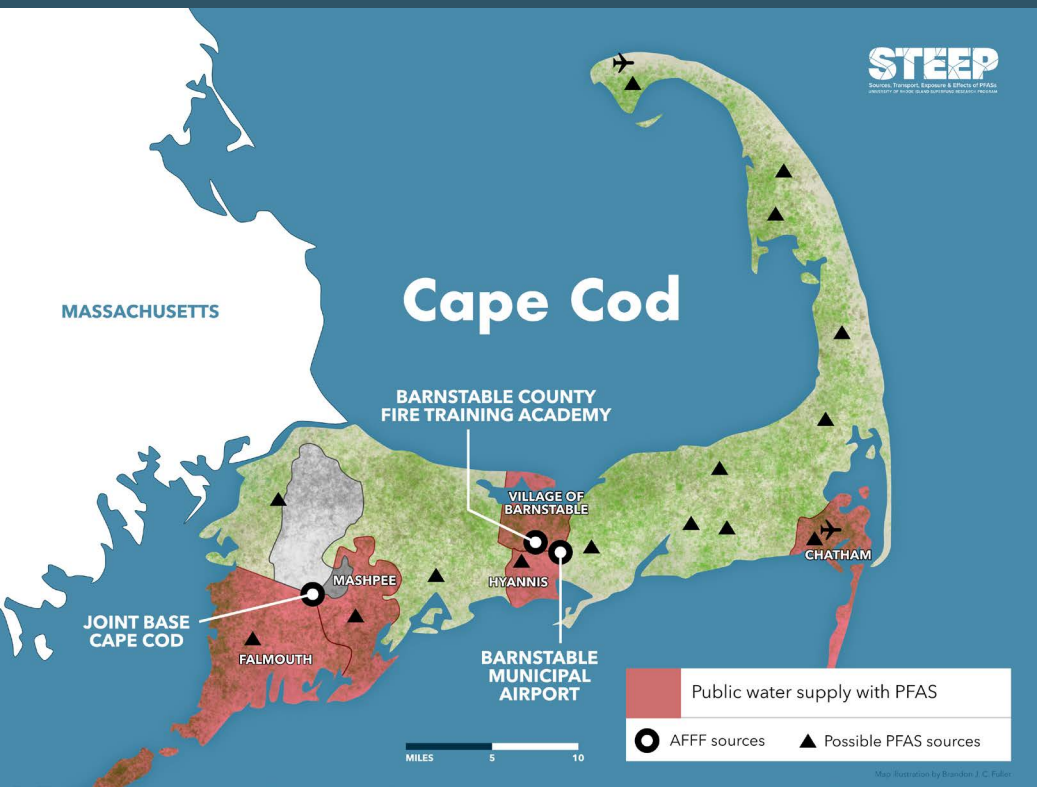
Exposure to some level of PFAS impacts the vast majority of people worldwide due to its ubiquitous presence in the environment and in a wide range of manufactured products and consumer goods; however, some communities akin to STEEP study sites experience increased exposure from secondary sources. In Cape Cod, the additional exposure to PFAS is linked to contaminated groundwater that finds its way to residents' tap water. The Faroe Islands fishing community experiences additional PFAS exposure linked to marine food intake, including the cultural tradition of consuming pilot whale meat that contains bioaccumulated PFAS from the marine food chain.

PFAS exposure is associated with a number of long-term health effects such as kidney cancer, higher cholesterol and fatty liver disease, above normal liver function tests, chronic kidney disease, obesity, diabetes, thyroid disease and other endocrine abnormalities, increased blood pressure and preeclampsia in pregnancy, and reduction of vaccine efficacy in regard to antibody responses that seems to be linked to a greater frequency and severity of at least some infectious diseases.

While continued and expanded study sites are critical to the specific research of PFAS as contributing to chronic health issues, some of the comorbidities, such as diabetes and obesity, often discussed in the context of COVID-19 risk, along with PFAS-associated immune system dysfunction, support the need for timely and expanded research and for the simultaneous reduction of these "forever chemicals."

"[Treating all PFAS as a group] is really the only way that we can be ahead of the curve. Rather than always realizing that a compound is toxic once it's already everywhere and we measure it on a remote ice-site somewhere in Greenland."

–Charlotte Wagner, *Massive Science*



Barnstable County, MA, is a Cape Cod area beloved for its sweeping coastline, quaint villages, and welcoming community ambiance. Groundwater on Cape Cod has been contaminated by PFAS from multiple sources. To date, these sources have been identified as fire training areas, airports, military bases, landfills, municipal wastewater, and septic systems. The spread of PFAS is exacerbated by Barnstable's location in an outwash plain with permeable soil. The result is that groundwater aquifers are highly susceptible to movement of contaminants from the surface of the ground—the place where surface water both contributes to aquifers and enters the food web. Once PFAS get into groundwater, they move with the groundwater and eventually can contaminate both public and private drinking water sources. Given these multiple inputs of PFAS and the unique geology of the area, there is an ongoing threat to Cape Cod's sole source aquifer that provides drinking water for 200,000 year-round and 500,000 summer residents.

The Faroe Islands consist of 18 inhabited volcanic islands, which are connected by a network of roads, ferries, subsea tunnels, and bridges. Located in the Atlantic Ocean between Norway and Iceland, these islands are a self-governing archipelago of the Kingdom of Denmark. With a population of slightly more than 50,000, this fishing community is situated in the heart of the Gulf Stream in the North Atlantic. In a generation, with the help of the fishing trade that accounts for approximately 20 percent of GDP, Faroese affluence has grown in the widespread use of technology and well-established infrastructure.

Beginning in 1985, study cohorts of ~2,300 Faroese children have been repeatedly re-examined to ascertain effects of mercury in their diet and later expanded to include PFAS. Consequently, the overall health threats from toxic chemicals to the current and future generations of Faroese are compelling and timely as reflections of widely occurring health risks.

Project 1: Environmental Fate & Transport

Environmental Engineering: Exposure assessment and chemometrics of PFAS

CENTRAL HYPOTHESIS:

Some geochemical and hydrological conditions facilitate PFAS transport and precursor transformation near contaminated sites, increasing their propensity to enter drinking water and fish.

Lead: **Elsie Sunderland,** Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)
Harvard John A. Paulson School of Engineering and Applied Sciences (SEAS)

"Our testing method was able to find these missing compounds that have been used by the chemical industry for more than 40 years."

–Elsie Sunderland, *Harvard Gazette*

OVERVIEW

More than 600 sites across the U.S. are contaminated by poly- and perfluoroalkyl substances (PFAS) but the extent of transport away from these sites and entry into human exposure pathways (drinking water and fish) is virtually unknown. This information is critical for assessing human health risks associated with exposures to PFAS from contaminated sites.

This project is investigating the diverse potential exposure pathways for PFAS. This work includes new measurements of PFAS present in water (surface waters, private wells, estuaries, tap water) and seafood in the Cape Cod/New England region and the Faroe Islands. The Joint Base Cape Cod (JBCC) is a contaminated Superfund site located on Cape Cod. As part of Project 1, STEEP researchers are investigating the fate of the aqueous film forming foam (AFFF) contaminated plume as it mixes with other PFAS sources and enters surface waters, downstream rivers and ultimately the marine environment. In collaboration with Project 4, researchers at University of Colorado Denver have investigated the uptake and bioconcentration of PFAS in laboratory fish. Further, Project 1 is investigating uptake and trophic magnification of PFAS in fish downstream of AFFF impacted locations.

Aims of this project include:

- The development of novel statistical methods to fingerprint profiles of PFAS measured in fish and drinking water to better understand contamination sources. As part of STEEP research, this technique was applied to better understand sources of human exposure to different demographic groups in the Faroe Islands and North America (Hu et al., 2018). In addition, this technique was used to understand how PFAS exposure sources for children in the Faroe Islands have changed over time (Dassuncao et al., 2018). Project 1 has further applied this technique to differentiate contamination in the environment from AFFF and other PFAS sources in surface waters on Cape Cod, MA (Ruyle et al., 2021). We have further developed a statistical technique for reconstructing major precursors in contemporary AFFF using information on the known transformations of PFAS precursors into terminal perfluoroalkyl acids (PFAA) and measured yields of precursors using the TOP assay (Ruyle et al., 2021).
- Better understanding of how environmental factors influence the transport and transformations of PFAS away from contaminated sites and into surface waters and the marine environment. When PFAS are transported away from source zones, they can cross

boundaries where surface-water and groundwater exchange occurs. This can result in groundwater contamination of surface waters and vice versa. These exchange areas display strong gradients in microbial activity, nutrients, dissolved oxygen, and other biogeochemical features that may impact PFAS transport and transformation and are found abundantly in the kettle pond topography of Cape Cod, MA. Project 1 has been particularly interested in how these interfaces and biogeochemical gradients influence the large quantities of polyfluoroalkyl precursors that degrade into terminal PFAS that are currently included in drinking water standards. In collaboration with the USGS, Project 1 research is investigating how biogeochemical factors influence PFAS transport and transformation along the hydrological flow path away from source zones. Results of this work have identified a strong seasonal fluctuation in PFAA concentrations at the boundaries for surface-water/groundwater exchange that affect downgradient concentrations. Precursor concentrations decline significantly by ~85% at these gradients compared to overlying lake water that has relatively stable precursor composition. Decreases in precursor concentrations were significantly and inversely associated with temperature and nitrate concentrations, suggesting a link to biological processes that mediate nitrogen cycling in this system (Tokranov et al., in review).

- Improved understanding of the propensity of different PFAS in the contaminated groundwater environment to enter fish and the accumulation in different tissues. The University of Colorado Denver and USGS have developed a mobile laboratory/water-quality characterization approach to assess PFAS bioconcentration. Researchers are investigating associations between PFAS accumulation in laboratory fish and endocrine disruption, metabolic effects and immune responses.

One of the major expected outcomes of this work is a better understanding of the spatial extent of elevated PFAS concentrations in fish and drinking water from contaminated sites, which will also improve our understanding of the vulnerability of exposed communities to PFAS contamination.

Progress to date

New method for measuring organofluorine accumulation at the surface of consumer products

It is well-established that targeted mass-spectrometry is only able to capture a small fraction of the PFAS present in environmental samples, which may result in underestimates of the magnitude of contamination present in the environment and human exposure. In this work, STEEP researchers used a widely available instrument available at most major research centers (x-ray photoelectron spectroscopy: XPS) to measure the total organofluorine present at the surface of common consumer products. The new method development allows for a true surface measurement that can identify surface coatings (much shallower depth than the method developed using particle-induced gamma ray emission: PIGE) and also depth profiles for PFAS present at the surface of products. This allows investigators to determine the homogeneity in PFAS application to the product. Results based on XPS measurements agree well with other studies that have shown consumer products contain many PFAS that are not detected using targeted measurement techniques.

Understanding the relative importance of diverse human exposure pathways for PFAS

Project 1 researchers have published numerous articles aimed at better identifying the relative importance of drinking water, seafood and consumer products as PFAS exposure sources (reviewed in Sunderland et al., 2019). PFAS concentrations were measured in archived drinking water samples from 1989/1990 at locations across the United States. This work revealed significant associations between PFAS concentrations in drinking water and serum PFAS concentrations in the background US population (away from contaminated sites), indicating the ubiquity of drinking water exposures to PFAS for many US individuals (Hu et al., 2019). Work conducted in collaboration with Project 2 in the Faroe Islands revealed that even in a remote Faroese fishing community, a large fraction of exposure originates from use of diverse consumer products containing PFAS and non-seafood sources (Dassuncao et al., 2018, Hu et al. 2018). Researchers showed that concentrations of legacy PFAS in the serum of children declined rapidly following the phase-out in PFOS production between 2000-2002, likely reflecting the elimination of PFOS and its precursors from consumer sources. These “steep” declines indicate the potential benefits from coordinated global action controlling production sources.

Trainee Heidi Pickard samples grasses from a dairy farm in Maine. Photo: Andrew Smith.

Bioaccumulation of PFAS in the marine food web

Research conducted collaboratively between Project 1 and Project 4 is providing new insights on accumulation of PFAS in seawater and uptake of PFAS in marine food webs (Zhang et al., 2019). This work suggests that contaminated submarine groundwater discharge may be a concern for some Northeast estuaries and delay recovery of PFAS contaminated sites when sources have been eliminated. It also suggests that short-chain PFAS precursors are contributing to higher than expected concentrations measured in marine plankton from the Northeastern Atlantic Ocean shelf and slope, which is likely to influence their accumulation in higher trophic level organisms consumed by humans and wildlife. Ongoing work is investigating how wastewater and groundwater inputs to Waquoit Bay, MA are affecting marine food web exposures to PFAS.

Tissue distribution of PFAS in marine mammals

Project 1 research, in collaboration with Project 3, has also been studying the toxicokinetics of PFAS distribution among the tissues of marine mammals and the controlling role of phospholipids for tissue distribution (Dassuncao et al., 2019). This research focused on pilot whales, which are an important exposure pathway for individuals in the Faroe Islands — the focus of Project 2 research. Results have shown preferential accumulation of long-chain PFAS in the brain of pilot whales, likely indicating facilitated transport mechanisms for some PFAS. In addition, high concentrations of the C-6 carboxylate were found in the liver, which is consistent with the role of specific binding proteins such as liver fatty acid binding proteins (FABP) affecting accumulation in different target sites. These hypotheses are being further evaluated by work associated with Project 3. Overall, this research has shown that a revised toxicokinetic model based on the phospholipid content of different organisms would improve the ability to represent tissue accumulation and bioaccumulation of PFAS.

Research highlight: Uptake and effects of PFAS in fish exposed to AFFF-contaminated groundwater

Project 1 experiments with the University of Colorado Denver, U.S. Geological Survey, and Project 4 on-site at an AFFF-contaminated groundwater plume have investigated multi-media uptake and effects of PFAS exposure. These experiments demonstrate distinct uptake profiles of PFAS mixtures in fish, mussels, and passive samplers. Specific PFAS compounds were detectable only in fish tissue, and not in water samples or by passive samplers. These findings have implications for environmental monitoring of PFAS concentrations. In collaboration with Project 3, evaluation of biomarkers in fish experimentally exposed to this AFFF-contaminated groundwater plume showed impaired sperm, elevated testicular histopathology, and disrupted liver lipids, paralleling observations in PFAS-exposed humans. Ongoing transcriptomic analysis of liver and testis mRNA aims to characterize the molecular regulatory networks mediating these reproductive and metabolic responses to environmental PFAS mixtures and their relationship to PFAS body-burden. Fish microbiome responses to PFAS have been amplified for 16S and metagenomic sequencing to provide a further linkage between PFAS aqueous concentrations and PFAS body burden. The relationship between molecular uptake mechanisms and tissue-specific PFAS concentrations is under investigation in collaboration with Project 3 and Project 4.

Research highlight: Isolating the AFFF Signature in Coastal Watersheds Using Oxidizable PFAS Precursors

Project 1 has developed a PFAS testing method to measure the PFAS source signature in watersheds on Cape Cod and reveal the presence of additional unknown organofluorine chemicals that have been previously overlooked. The method combines measurements of terminal compounds as well as oxidizable precursor and extractable organofluorine. Measured concentrations are used in statistical source attribution models that

predict the perfluorinated chain length and origin of precursors as well as reveal the predominant PFAS signatures in six adjacent watersheds on Cape Cod with and without upstream fire-fighting foam use. Project 1 found that while fire-fighting foams contributed to much higher concentrations of terminal PFAS and precursors in downstream watersheds, an additional 50% of PFAS compounds was identified for the first time from currently unknown sources. The team is preforming follow-up studies to try to identify these PFAS and their origins. The study was published earlier this year in *Environmental Science & Technology*, and was highlighted in the *Harvard Gazette*, *Cape Cod Times* and *Boston Globe*. It was also selected as an NIEHS extramural publication of the month.

Machine learning model for identifying the susceptibility of private wells to PFAS contamination

More than 40 million US individuals rely on private wells for their drinking water but monitoring is time consuming and costly. Project 1 researchers have therefore been investigating the utility of using existing state level PFAS data to train and validate machine learning models that predict where high PFAS levels are likely to occur. Pilot work toward this aim was conducted using thousands of private well PFAS measurements from the state of New Hampshire (NH) in combination with geospatial information on source locations and environmental properties that affect PFAS transport. Existing monitoring data were used to train statistical models that predict locations where private wells are likely to have detectable concentrations. This research was published in *Environmental Science & Technology Letters* in 2021 (Hu et al., 2021). A second phase of this project using newer data from NH and the states of MI and NJ is now being planned.

Plan for the final duration of the current award

- Publish first iteration of a mechanistic model for PFAS bioaccumulation in aquatic food webs (Jennifer Sun).
- Publish data on PFAS in NH lakes and new method for measuring precursors and EOF in fish tissue (Heidi Pickard).
- Evaluate the agronomic exposure pathway for PFAS in collaboration with the state of ME (Heidi Pickard and Harvard College undergraduate Jordan Daigle).
- Further explore the source of unidentified organofluorine in Cape Cod coastal watersheds (Bridger Ruyle).
- Measure targeted PFAS, precursors and total organofluorine in fish from Waquoit Bay (Heidi Pickard).
- Publish a new atmospheric simulation for PFAS deposition in the Northeastern US using the GEOS-Chem model (Colin Thackray/Lara Schultes).
- Participate in planning for the pending STEEP continuation.

Bridger Ruyle collects eels from Upper Quashnet River. Photo: Sunderland Lab.

PROJECT 1 SELECTED ACCOMPLISHMENTS

Manuscripts

X.C. Hu, B. Ge, **B. Ruyle**, **J. Sun**, **E.M. Sunderland**. 2021. A statistical approach for identifying private wells susceptible to PFAS contamination. *Environmental Science & Technology Letters*. 8(7): 596-602.

Ruyle B.J., **Thackray C.P.**, McCord J.P., Strynar ,M.J., Mauge-Lewis K.A., Fenton S.E., **Sunderland E.M.** 2021. Reconstructing the composition of poly- and perfluoroalkyl substances (PFAS) in contemporary aqueous film forming foams. *Environmental Science & Technology Letters.* 8(1): 59-65.

Young A.S., Sparer-Fine E.H., **Pickard H.M.**, **Sunderland E.M.**, Peaslee G.F., Allen J.G. 2021. Per- and polyfluoroalkyl substances (PFAS) and total fluorine in fire station dust. *Journal of Exposure Science and Environmental Epidemiology*. https://doi.org/10.1038/s41370-021-00288-7

Ruyle B.J., **Pickard H.M.**, LeBlanc D.R., **Tokranov A.K.**, **Thackray C.P.**, **Hu X.C.**, Vecitis C.D., **Sunderland E.M.** 2021. Isolating the AFFF signature in coastal watersheds using oxidizable PFAS precursors and unexplained organofluorine. *Environmental Science and Technology.* 55(6): 3686-3695.

Tokranov A.K., LeBlanc D.R., **Pickard H.M**., **Ruyle B.J.**, Barber L.B., Hull R.B., **Sunderland E.M.**, Vecitis C.D. 2021. Surface-water/groundwater boundary effect on seasonal PFAS concentrations and PFAA precursor concentrations. *Environmental Science Processes and Impacts.* In review.

De Silva A.0., Armitage J.M., Bruton T.A., **Dassuncao C.**, Heiger-Bernays W., **Hu X.C.**, Karrman A., Ng C., **Robuck A.**, Sun M., Webster T.F., **Sunderland E.M.** 2021. PFAS Exposure Pathways for Humans and Wildlife: A Synthesis of Current Knowledge and Key Gaps in Understanding. *Environmental Toxicology and Chemistry.* 40 (3): 631-657.

PROJECT 1 TRAINEES

Heidi Pickard, Ph.D. Candidate, Harvard SEAS
Bridger Ruyle, Ph.D. Candidate, Harvard SEAS
Charlotte Wagner, Ph.D. Candidate, Harvard SEAS
Jennifer Sun, Ph.D. Candidate, Harvard SEAS
Lara Schultes, Postdoctoral Fellow, Harvard SEAS

PROJECT 1 GRADUATES

Andrea Tokranov, Ph.D., Harvard SEAS, June 2019; Scientist, US Geological Survey
Clifton Dassuncao, Ph.D., HSPH, May 2018; Scientist, Eastern Research Group
Xindi (Cindy) Hu, Ph.D., HSPH, May 2018; Scientist, Mathematica Policy Research, Inc.
Charlotte Wagner, Ph.D., Harvard SEAS, May 2021; Scientist, Energy and Environmental Modeler, Stockholm Environment Institute

Sunderland Lab members use a seine net to collect fish from Moody Pond. Photo: Sunderland Lab.

Project 2: Childhood Risk

Epidemiological Study: Inflammation and metabolic changes in children developmentally exposed to PFAS

CENTRAL HYPOTHESIS:

Dietary exposure to PFAS during fetal development and childhood can interfere with immune system development and metabolism and thereby pave the way for later disease development.

Lead: **Philippe Grandjean,** Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)

Clinical Lead: **Pál Weihe, MD,** Adjunct Professor at The University of the Faroe Islands and Head of the Department of Occupational Medicine and Public Health

Key Personnel: **Carmen Messerlian,** Harvard T.H. Chan School of Public Health, Department of Environmental Health and Department of Epidemiology (HSPH)

OVERVIEW

Poly- and perfluoroalkyl substances (PFAS) are widely used industrial chemicals, but the existence of human PFAS exposures from contaminated sites and bioaccumulation in food-chains and consumer products was discovered less than 20 years ago. Only now are the adverse health effects becoming better known. Recent evidence suggests that current PFAS exposures may cause adverse effects on the immune system and other sensitive tissues and organs, even at exposures far below provisional exposure limits. This is particularly true in regard to early-life exposure to PFAS that may contribute to the development of metabolic diseases, including obesity and type 2 diabetes. PFAS can also decrease antibody response to certain childhood vaccinations. In addition to the vulnerability of early-life functional development, PFAS are transferred through the placenta and via breast milk, thus potentially exposing the most sensitive life stages to highly elevated PFAS amounts.

Relying on a birth cohort in the Faroe Islands that was already established with support from the National Institute of Environmental Health Sciences (NIEHS), this project is utilizing exposure and outcome data covering a 9-year span to determine possible links between prospective PFAS exposure profiles, immune dysfunction, and metabolic abnormalities. Due to the homogeneity of the Faroese population, the wide range of exposures, and the high participation rate in the clinical follow-up, this epidemiological setting represents advantages that would be nearly impossible to match anywhere else.

The data analysis takes into account additional factors, including exposures to other environmental chemicals, sex of the child, and diet. Overall, our prospective approach will allow us to contribute important documentation on early developmental stages for possible use in PFAS risk characterization in U.S. populations and internationally.

Faroese child from study cohort with Dr. Frodi Debes. Photo: Philippe Grandjean collection.

Progress to date

Through interdisciplinary collaboration and a shared commitment to bettering the health of communities impacted by environmental PFAS contamination, the STEEP Center team has made steady and promising progress in upholding the commitment to the Cape Cod and Faroe Island communities while advancing the science on PFAS exposure.

This epidemiological project is a prospective study which takes advantage of a birth cohort (N = 490) established in the Faroe Islands, a North Atlantic fishing community where early-life exposures to persistent environmental pollutants, such as PFAS, have been linked to immunotoxicity, obesity and related metabolic conditions in previous epidemiological studies. The cohort was generated from consecutive births between 2007 and 2009 and is the largest and most thoroughly examined group of PFAS-exposed children followed since birth. Progress to date includes:

- Completion of all clinical exams and blood work of the cohort members (8-9 years) who accepted the invitation to participate and re-consented (N = 407, 210 boys and 197 girls; 83% participation). Also, 385 DXA scans have been completed to assess body fat content and bone mass. All clinical data have been entered into the database. Routine blood tests and PFAS analyses have been completed, and advanced statistical analyses of vaccine antibodies and metabolic biomarkers have been done.
- At current PFAS exposure levels (where PFHxS, PFOS, and PFOA are much lower than in the previous cohort), vaccine antibody levels appear not as strongly affected by PFAS as in previous studies. We are therefore merging the data with those from the previous cohort. Still, the new cohort shows statistically significant inverse associations between the pre-booster diphtheria antibody and PFOA both prenatally and at age 5, and stronger associations between PFAS exposures and post-booster antibody concentrations.
- Assessment of lipid metabolism, including serum-cholesterol parameters, shows increased lipids at higher PFAS exposures at the ages of 5 and 9 years, with some sex differences. Funding has been received to measure cholesterol subfractions (such as the HDL that contains apoC3, linked to cardiovascular disease risk). In addition, adipokines have been measured, i.e., the cytokines that originate from adipose tissue. Thus, changes in leptin, the leptin receptor, and resistin at age 9 years were primarily linked with serum-PFAS concentrations at 18 months and at 5 and 9 years, whereas links to prenatal PFAS exposures were mostly null. Advanced modeling of infancy-age serum-PFAS concentrations and resistin at age 9 years shows inverse associations with the early postnatal PFAS exposure (mainly dependent on duration of breastfeeding). These findings are important regarding postnatal programming of metabolic functions.
- Because of the endocrine disrupting properties of PFAS, research has focused on the areal bone mineral density (aBMD) obtained by DXA scans. Preliminary findings show the strongest inverse association for PFOA at age 9 years (cross-sectional), but significant associations were also seen for PFAS measured in serum at ages 18 months and 5 years. Mediation analysis suggests that 18-month PFAS exposures may affect both aBMD and body fat, while age-5 exposures were independent of BMI and body fat in regard to the decreased aBMD. These findings support the notion that a PFAS-associated loss in BMD may begin in childhood.
- Serum-PFAS analytical methods have been upgraded and optimized on a new and more sensitive UPLC-MS/MS system comprising a Thermo Scientific EQuan MAX module for online solid-phase extraction and a TSQ Quantiva triple quadropole mass spectrometer. All exposure biomarker analyses have been completed at a high quality level.

Plan for the final duration of the current award

- Complete the analysis of clinical data, including DXA scans, in regard to PFAS exposure biomarkers and serum biomarkers.
- Extend advanced statistical data analyses, including calculation of derived parameters and structural equation models, with benchmark dose results, in collaboration with subcontractors. These analyses will also include estimated PFAS exposures during infancy.
- Participate in planning for the pending STEEP continuation.

"At the end of the breast-feeding period, the child may have a serum concentration of PFAS that may be 10 times higher than the mother's because the mother is essentially eliminating PFAS from her body. Her serum concentrations go down, and the child cannot excrete them. So, they just keep on building up in the baby's body."

–Philippe Grandjean, *NOVA PBS*

PROJECT 2 GRADUATES

Damaskini Valvi, Postdoctoral Researcher, Harvard; recently accepted a position at the Mount Sinai School of Medicine as an Assistant Professor in Environmental Medicine & Public Health. https://www.mountsinai.org/profiles/valvi-damaskini

Annelise Blomberg, Postdoctoral Research Fellow, Harvard T.H. Chan School of Public Health; Research Engineer, Faculty of Medicine, Division of Occupational and Environmental Medicine, Lund University.

Yu-Hsuan Aria Shih, Postdoctoral Research Fellow, Harvard T.H. Chan School of Public Health; Manager, Health Economics and Outcomes Research, Novartis.

PROJECT 2 SELECTED ACCOMPLISHMENTS

Manuscripts

Birukov A., Andersen L.B., Andersen M.S., Nielsen J.H., Nielsen F., Kyhl H.B., Jørgensen J.S., **Grandjean P.**, Dechend R., Jensen T.K. 2021. Exposure to perfluoroalkyl substances and blood pressure in pregnancy among 1436 women from the Odense Child Cohort. *Environ Int.* 151:106442. PMID: 33610053

Blomberg A.J., **Shih Y.H.**, **Messerlian C.**, Jørgensen L.H., **Weihe P.**, **Grandjean P.** 2021. Early-life associations between per- and polyfluoroalkyl substances and serum lipids in a longitudinal birth cohort. *Environ Res.* 200:111400. PMID: 34081971.

Christensen J.V.R., Bangash K.K., **Weihe P.**, **Grandjean P.**, Nielsen F., Jensen T.K., Petersen M.S. 2021. Maternal exposure to perfluoroalkyl chemicals and anogenital distance in the offspring: a Faroese cohort study. *Reprod Toxicol.* S0890-6238(21)00101-5. PMID: 34182087.

Dalsager L., Christensen N., Halekoh U., Timmermann C.A.G., Nielsen F., Kyhl H.B., Husby S., **Grandjean P.**, Jensen T.K., Andersen H.R. 2021. Exposure to perfluoroalkyl substances during fetal life and hospitalization for infectious disease in childhood: A study among 1,503 children from the Odense Child Cohort. *Environ Int.* 149:106395. PMID: 33508532.

Gardener H., Sun Q., **Grandjean P**. 2021. PFAS concentration during pregnancy in relation to cardiometabolic health and birth outcomes. *Environ Res.* 192:110287. PMID: 33038367

Grandjean P., Timmermann C.A.G., Kruse M., Nielsen F., Vinholt P.J., Boding L., Heilmann C., Mølbak K. 2020. Severity of COVID-19 at elevated exposure to perfluorinated alkylates. *PLoS One.* 15(12):e0244815. PMID: 33382826.

Jensen R.C., Andersen M.S., Larsen P.V., Glintborg D., Dalgård C., Timmermann C.A.G., Nielsen F., Sandberg M.B., Andersen H.R., Christesen H.T., **Grandjean P.**, Jensen T.K. 2020. Prenatal Exposures to Perfluoroalkyl Acids and Associations with Markers of Adiposity and Plasma Lipids in Infancy: An Odense Child Cohort Study. *Environ Health Perspect.* 128(7):77001. PMID: 32628516.

Shih Y.H., **Blomberg A.J.**, Bind M.A., Holm D., Nielsen F., Heilmann C., **Weihe P.**, **Grandjean P.** 2021. Serum vaccine antibody concentrations in adults exposed to per- and polyfluoroalkyl substances: A birth cohort in the Faroe Islands. *J Immunotoxicol.* 18(1):85-92. PMID: 34143710

Timmermann C.A.G., Jensen K.J., Nielsen F., Budtz-Jørgensen E., van der Klis F., Benn C.S., **Grandjean P.**, Fisker A.B. 2020. Serum Perfluoroalkyl Substances, Vaccine Responses, and Morbidity in a Cohort of Guinea-Bissau Children. *Environ Health Perspect.* 128(8):87002. PMID: 32772733.

Valvi D., Højlund K., Coull B.A., Nielsen F., **Weihe P.**, **Grandjean P.** 2021. Life-course exposure to perfluoroalkyl substances in relation to markers of glucose homeostasis in early adulthood. *J Clin Endocrinol Metab.* dgab267. PMID: 33890111

Waterfield G., Rogers M., **Grandjean P.**, Auffhammer M., Sunding D. 2020. Reducing exposure to high levels of perfluorinated compounds in drinking water improves reproductive outcomes: evidence from an intervention in Minnesota. *Environ Health.* 19(1):42. PMID: 32321520

Xiao C., **Grandjean P.**, **Valvi D.**, Nielsen F., Jensen T.K., **Weihe P.**, Oulhote Y. 2020. Associations of Exposure to Perfluoroalkyl Substances With Thyroid Hormone Concentrations and Birth Size. *J Clin Endocrinol Metab.* 105(3):735-45. PMID: 31665456.

Presentations

Grandjean P. *PFAS in water: innocuous or injurious?* PFAS in Our World: What We Know and What We Can Do virtual conference. 13-14 October, 2020.

Grandjean P. *Adverse effects of PFAS on immune system health.* Alaska's Collaborative on Health and the Environment webinar, 2 December, 2020.

Grandjean P. *PFAS in water: innocuous or injurious?* NH Safe Water Summit. New Hampshire Safe Water Alliance, 30 January, 2021.

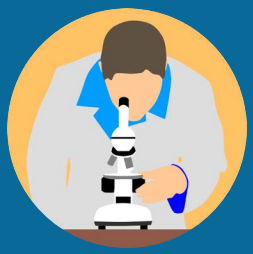
Grandjean P. *How little is still too much: Limits for PFAS in drinking water* (keynote presentation). Fate of PFAS: From Groundwater to Tap Water, National Ground Water Association, 22-23 June 2021.

Grandjean P. *Panel member.* PFAS conference. Environmental Working Group, 14 July, 2021.

Messerlian C. *Perfluoroalkyl Substances and Immune Function in Children and Adolescents*. Invited Presentation. Sources, Transport, Exposure and Effects of Perfluoroalkyl Substance (STEEP) Science Day, Barnstable, MA, March 2021.

Messerlian C. *Health Effects of Exposure to PFAS.* Invited Webinar, Northeast Waste Management Officials' Association (NEWMOA), Boston, MA, March 2021.

Dr. Philippe Grandjean, co-lead of STEEP.



Project 3: Metabolic Effects

PFAS compounds induce metabolic abnormalities in rodents and cells

CENTRAL HYPOTHESIS:

PFAS exposure leads to metabolic abnormalities in rodents and cells, which can be linked back to preferential sorption of PFAS to biomolecules.

Co-lead: **Angela Slitt,** URI College of Pharmacy (Pharm)

Co-lead: **Geoffrey Bothun,** URI College of Engineering (COE)

OVERVIEW

Human exposure to poly- and perfluoroalkyl substances (PFAS) has been linked to immunotoxicity and cancer as well as metabolic disorders and cholesterol levels. Specific to metabolic disorders, PFAS are known to concentrate in the liver and links have been established between PFAS serum levels, specifically perfluorooctanoic acid (PFOA) and perfluorosulfonic acid (PFOS), and liver injury. While these findings are insightful, these two common PFAS chemicals represent only a fraction of PFAS that exist within the contaminated sites. Mechanisms driving biological response to PFAS compounds are still being investigated.

This project will:

- Address whether environmental exposure to PFAS contributes an additional increase in risk for obesity, obesity-induced fatty liver disease, and metabolic hormone disorders in cells and mice.
- Test the hypotheses that (1) PFAS exposure increases diet-induced fatty liver disease and inflammation, and (2) that the biological changes in the liver can be correlated with the body's response to PFAS.
- Identify the physicochemical and partitioning behaviors of PFAS that contribute to bioaccumulation and can explain PFAS behavior in tissues.

These project results will inform how PFAS exposure impacts risk factors common in the U.S. population (e.g., diet and obesity).

Angela Slitt (P3) and Naomi Pajarillo (undergraduate mentee) prepare solutions for a pharmacokinetic study on mice. Photo: Emily Kaye.

Progress to date

Slitt Lab

- Completed Aim 1, with additional studies to include proteomics analysis to reveal how 12 PFAS impact the process of adipogenesis. A revised manuscript on the hepatocyte results has been re-submitted to *ES&T* (IF=7.1). A second manuscript that details evaluation of 12 PFAS on adipogenesis and alteration of the adipocyte proteome has been submitted to *Toxicology* and is under review. A third manuscript that describes induction of gene expression with PFAS mixtures is currently in preparation. Major findings from the work were that PFAS, especially PFNA and those still in commercial use, can 1) induce adipogenesis and shift the adipocyte proteome and 2) induce lipid accumulation and gene expression signatures in human hepatocytes at exposure-relevant concentrations.
- Aim 2 has been completed. A revised manuscript detailing the major findings has been submitted to *Toxicology* and is under review. Several other manuscripts further detailing findings from Aim 2 are currently being written and will be submitted soon. A major finding from the manuscript was that maternal diet influenced PFAS distribution and effects in pups. In addition, PFAS mixtures administered maternally behaved differently than individual PFAS in the dam and pup.
- Several other PFAS-related manuscripts that were underway when STEEP was awarded have also been published, illustrating that PFHxS markedly shifts the serum lipidome and that diet-PFAS interactions occur in adult mice.
- Supplemental work funded through an NIA initiative for Alzheimer's disease research has resulted in one publication, illustrating that PFOS can upregulate ApoE, a biomarker for Alzheimer's Disease, in cells and cortex of mice.
- Partnership formed with Pfizer's Drug Metabolism Pharmacokinetics Group to jointly mentor Sangwoo Ryu, a full-time Pfizer employee. Sangwoo is applying Pfizer high-throughput screening assays to better understand physiochemical characteristics of PFAS that contribute to tissue distribution and elimination half-life in support of Project 3 renewal.
- Juliana Agudelo traveled to the EPA in February 2021 to measure PFAS in human livers and serum in Dr. Mark Strynar's laboratory to fulfill her KC Donnelly Award.
- Additional data have been generated to support the hypotheses for the renewal application and will be submitted as supplemental data for review. This includes demonstrating that numerous PFAS still in commercial use are high affinity substrates for the BCRP/ABCG2 transporter.
- Collaboration formed with Dr. Carmen Messerlian (Harvard University, Project 2). Dr. Messerlian is an epidemiologist with expertise on PFAS whose research group has mined the NHANES database to search for PFAS-fruit juice interactions. The findings of this research have been presented at the 33rd Annual Conference of the International Society for Environmental Epidemiology.

Bothun Lab

- A critical analysis has been conducted of fluorescence-based mathematical quenching models that continue to be used to determine PFAS binding to albumin proteins. A manuscript is currently under review in the journal *Chemosphere* (led by trainee J. Alesio). The analysis shows that 1) PFAS binding to bovine serum albumin (BSA) leads to static and dynamic quenching mechanisms, 2) PFAS binding to BSA is cooperative where PFAS bind can enhance or restrict further PFAS binding, and 3) that binding based on quenching agrees with equilibrium dialysis measurements for short PFAS, but greatly underpredicts for long PFAS.
- Differential scanning fluorimetry has been developed as a means of rapidly assessing PFAS-protein and fatty acid-protein binding simultaneously with conformational changes in protein structure. PFOA and PFNA outcompete their fatty acid analogs for BSA binding, but PFDA and decanoic acid bind with similar affinity due to steric hindrance in accessing the binding site. A manuscript led by trainee J. Alesio is in preparation.
- The Bothun Lab is conducting what is believed to be the first study of the effect of lipid charge on PFAS partitioning into cellular membranes using mixtures of neutral and negatively charged lipids. One manuscript has been finalized and will be submitted this summer and a second manuscript is pending the final experimental work being conducted this summer.

Trainee Juliana Agudelo extracts PFAS from human serum while working at US EPA on her KC Donnelly Externship. Photo: Mark Strynar.

Plans for the final duration of the current award

- Submit the manuscript in preparation reporting Aim 1 results on PFAS mixtures and hepatocytes.
- Publish the additional resulting studies for Aim 2, which include transcriptomic and proteomic analysis of liver, lung, and brain from mouse pups developmentally exposed to PFOS, PFOA, PFHxS, or a PFOS/PFOA/PFHxS mixture.
- Perform additional studies that will support the resubmission effort (i.e., FABPKO mouse studies, transporter assays, and apple juice extract studies).
- Continue to publish the remaining three to four manuscripts related to the Bothun Lab's research.
- Determine PFAS partitioning into mammalian cell membranes (e.g., hepatocytes) and membrane extracts, and identify PFAS-lipid interactions.
- Participate in planning for the pending STEEP continuation.

PROJECT 3 TRAINEES

Current Trainees

Jessica Alesio (formerly Orr), PhD Student, URI Engineering
Juliana Agudelo, PhD Student, URI Pharmacy
Emily Kaye, MS Student, URI Pharmacy
Sadegh Modaresi, URI Pharmacy
Sangwoo Ryu, URI Pharmacy and Pfizer Global Research

Trainee Milestones

Jessica Alesio passed her comprehensive examination on December 2021 to become a PhD candidate.

Graduates

Michael Fedorenko, MS, URI Engineering Fall 2019; Project Engineer, Sustainment and Restoration Services
Emily Marques PhD URI Pharmacy Spring 2020; Postdoctoral Fellow, UMass Amherst, School of Public Health
Aleksandra Naumann, MS, URI Engineering Spring 2020; Health Research Associate, Institute of Machine Tools and Production Technologies, Technische Universität Braunschweig
Marisa Pfohl, PhD, URI Pharmacy Fall 2019; Postdoctoral Fellow/Toxicologist, US EPA 2019-2021; Physical Scientist, US EPA 2021-present

Awards and Recognition

Naomi Parajillo, a URI undergraduate researcher in Dr. Slitt's laboratory and mentee of Juliana Agudelo, was awarded the prestigious Robert L. Carothers Servant Leadership Award in May 2021.

Angela Slitt was the recipient of the 2021 URI Foundation & Alumni Engagement Excellence Award in Scholarly Excellence

Angela Slitt's expert testimony to the Rhode Island State Senate was covered by the *Providence Journal:*
https://www.providencejournal.com/story/news/local/2021/02/26/action-urged-ban-forever-chemicals-food-packaging-and-takeout-containers/6833994002/

Angela Slitt and team were featured in a URI press release that was picked up by 14 different news sources in March 2021.
Providence Journal:
https://www.providencejournal.com/story/news/coronavirus/2021/03/16/uri-researchers-have-developed-saliva-based-covid-test/4700602001
Boston Globe:
https://www.bostonglobe.com/2021/03/16/metro/saliva-based-covid-19-test-be-submitted-emergency-use-authorization-with-fda/
RI NPR The Public's Radio

PROJECT 3 SELECTED ACCOMPLISHMENTS

Manuscripts

Pfohl M., DaSilva N.A., **Marques E.**, **Agudelo J.**, Liu C., Goedken M., **Slitt A.L.**, Seeram N.P., Ma H. 2021. Hepatoprotective and anti-inflammatory effects of a standardized pomegranate *(Punica granatum)* fruit extract in high fat diet-induced obese C57BL/6 mice. *Int J Food Sci Nutr*, 72:499-510. doi: 10.1080/09637486.2020.1849041. Epub 2020 Nov 18. PMID: 33203257.

Hamilton M.C., Heintz M.M., **Pfohl M.**, **Marques E.**, Ford L., **Slitt A.L.**, Baldwin W.S. 2021. Increased toxicity and retention of perflourooctane sulfonate (PFOS) in humanized CYP2B6-Transgenic mice compared to Cyp2b-null mice is relieved by a high-fat diet (HFD). *Food Chem Toxicol,* 152:112175. doi: 10.1016/j.fct.2021.112175. PMID: 33838175; PMCID: PMC8154739.

Marques E., **Pfohl M.**, Auclair A., Jamwal R., Barlock B.J., Sammoura F.M., Goedken M., Akhlaghi F., **Slitt A.L.** 2020. Perfluorooctanesulfonic acid (PFOS) administration shifts the hepatic proteome and augments dietary outcomes related to hepatic steatosis in mice. *Toxicol Appl Pharmacol*, 408:115250. doi: 10.1016/j.taap.2020.115250. PMID: 32979393.

Pfohl M., Ingram L., **Marques E.**, Auclair A., Barlock B., Jamwal R., Anderson D., Cummings B.S., **Slitt A.L.** 2020. Perfluorooctanesulfonic Acid and Perfluorohexanesulfonic Acid Alter the Blood Lipidome and the Hepatic Proteome in a Murine Model of Diet-Induced Obesity. *Toxicol Sci,* 178(2):311-324. doi: 10.1093/toxsci/kfaa148. PMID: 32991729; PMCID: PMC7751193.

Pfohl M., **Marques E.**, Auclair A., Barlock B., Jamwal R., Goedken M., Akhlaghi F., **Slitt A.L.** 2021. An 'Omics Approach to Unraveling the Paradoxical Effect of Diet on Perfluorooctanesulfonic Acid (PFOS) and Perfluorononanoic Acid (PFNA)-Induced Hepatic Steatosis. *Toxicol Sci,* 180(2): 277-294. doi: 10.1093/toxsci/kfaa172. PMID: 33483757; PMCID: PMC8041463.

Fedorenko M., **Alesio J.**, Fedorenko A., **Slitt A.L.**, **Bothun G.D.** 2021. Dominant entropic binding of perfluoroalkyl substances (PFASs) to albumin protein revealed by 19F NMR. *Chemosphere,* 263:128083. doi: 10.1016/j.chemosphere.2020.128083. PMID: 33297081.

Salter D.M., Wei W. Nahar P.P., **Marques E.**, **Slitt A.L.** 2021. Perfluorooctanesulfonic acid (PFOS) thwarts the beneficial effects of calorie restriction and Metformin. *Toxicol Sci,* doi: 10.1093/toxsci/kfab043, PMID: 33844015.

Amaeze O.*, Eng H., Horlbogen L., Varma M.V.S., **Slitt A.L.** 2021. Cytochrome P450 Enzyme Inhibition and Herb-Drug Interaction Potential of Medicinal Plant Extracts Used for Management of Diabetes in Nigeria. *Eur J Drug Metab Pharmacokinet,* doi: 10.1007/s13318-021-00685-1. Online ahead of print. PMID: 33844145. *Ogo Amaeze was a Fulbright Scholar. Reagent overage from Project 3 was used to complete aspects of this publication.

Marques E.S., **Pfohl M.**, Wei W., Tarantola G., Ford L., Amaeze O., **Bothun G.**, **Slitt A.L.** Replacement per- and polyfluoroalkyl substances (PFAS) are potent modulators of lipogenic and drug metabolizing gene expression signatures in primary human hepatocytes. *Environmental Science and Technology, resubmitted with revisions, August 2021.*

Marques E.S., **Agudelo J.**, **Kaye E.**, **Modaresi S.**, **Pfohl M.**, Wei W., Polunas M., Goedken M., **Slitt A.L.** The role of maternal high fat diet on mouse pup metabolic endpoints following perinatal PFAS and PFAS mixture exposure. *Toxicology, revision resubmitted, under review.*

Alesio J., **Slitt A.L.**, **Bothun G.D.** Critical new insights into the binding of poly- and perfluoroalkyl substances (PFAS) to albumin protein, *Chemosphere, under first revision*.

Alesio J., Pan, A., **Bothun G.D.** Perfluoroalkyl carboxylates and sulfonates lead to membrane ordering in the hydrocarbonoclastic bacteria *Alcanovorax Borkumensis* without impacting growth. Environmental Science and Technology. *In preparation.*

"There are over 3,000 [PFAS chemicals] on the market and it's too challenging to regulate and understand them one by one."

–Angela Slitt, *ecoRI News*

Poster Presentations

Sangwoo Ryu, Application of Presaturation Equilibrium Dialysis Binding for Various PFAS to Plasma, Tissue, and Breast Milk, *accepted*, SETAC North America 42nd Annual Meeting, November 2021.

Zhang Y., Mustieles V., Wang Y., Sun Y., Bibi Z., **Slitt A.L.**, **Messerlian C**. Dietary intake and blood concentrations of folate and folic acid in relation to serum per- and polyfluoroalkyl substances (PFAS) concentrations, *accepted for poster presentation,* ISEE, August 2021.

Zhang Y., **Agudelo J.**, Parajillo N., Mustieles V., Sun Y., Wang Y., **Slitt A.L.**, **Messerlian C.** Using a translational research paradigm to investigate dietary intake of fruit juice on per- and polyfluoroalkyl substances (PFAS) concentrations, *accepted for poster presentation,* ISEE, August 2021.

Bothun G.D., **Naumann A.**, **Alesio J. A.** Perfluoroalkyl Substances (PFASs) Partition into Bacterial Cell Membranes and Cause Unexpected Lipid Ordering, AIChE annual fall meeting, virtual (Nov 2020).

Alesio J., **Bothun G.D.** Poly- and Perfluoroalkyl Substances (PFAS) Bind to Proteins and Stiffen Membranes: Using Physicochemical Properties to Characterize Human and Environmental Effects, AIChE annual fall meeting, virtual (Nov 2020).

Alesio J., **Crisalli A.**, Cho, B., **Bothun G.D.** Binding of Perfluoroalkyl Substances (PFAS) to Serum Albumins: A Comparison of Human and Bovine Serum Albumins, AIChE annual fall meeting, virtual (Nov 2020).

Alesio J., **Bothun G.D.** Perfluoroalkyl Substances (PFAS) Affect the Membrane Fluidity of *Alcanivorax Borkumensis* but Do Not Delay Growth, AIChE annual fall meeting, virtual (Nov 2020).

Oral Presentations

Bothun G.D., **Fedorenko M.**, **Alesio J.**, Fedorenko, A., **Slitt, A. L.** Dominant Entropic Binding of Perfluoroalkyl Substances (PFASs) to Albumin Protein Revealed by 19F NMR, AIChE annual fall meeting, virtual (Nov 2020).

Zhang Y., Mustieles V., Sun Y., Vagios S., **Slitt A.L.**, Wang Y.X., **Messerlian C.**, Serum per- and polyfluoroalkyl substance concentrations and common cold among children and adolescents in NHANES 2013-2014. Accepted Oral Presentation, Society for Epidemiological Research 2021.

Zhang Y., Mustieles V., Sun Y., Vagios S., **Slitt A.L.**, Wang Y.X., **Messerlian C.** Serum per- and polyfluoroalkyl substance concentrations and common cold among children and adolescents in NHANES 2013-2014. Accepted Oral Presentation, Society for Pediatric and Perinatal Epidemiologic Research 2021.

Zhang Y., Mustieles V., Wang Y.X., Sun Y., Bibi Z., **Slitt A.L.**, **Messerlian C.** Dietary intake and blood concentrations of folate and folic acid in relation to serum per- and polyfluoroalkyl substances (PFAS) concentrations. Accepted Presentation, International Society for Environmental Epidemiology 2021.

Zhang Y., **Agudelo J.**, Parajillo N., Mustieles V., Sun Y., Wang Y.X., **Slitt A.L.**, **Messerlian C.** Using a translational research paradigm to investigate dietary intake of fruit juice on per- and polyfluoroalkyl substances (PFAS) concentrations. Accepted Presentation, International Society for Environmental Epidemiology 2021.

Invited Presentations

Angela Slitt, June 2021, National Firefighter Cancer Symposium, invited speaker "Cell to Community: The Nexus of Basic Sciences and Population Health"

Angela Slitt, February 2021, KCU-Joplin Basic Science Department Seminar Series, invited speaker "Developing a SARS-CoV-2 nucleic acid test in the academic environment: The wild west meets regulatory science"

Angela Slitt, University of Calgary, April 2021, Invited Speaker, "Developing a SARS-CoV-2 nucleic acid test in the academic environment: The wild west meets regulatory science"

Other Activities

- **Slitt** provided written and expert testimony related to RI Senate Bills: PFAS in Drinking Water, Groundwater, and Surface Waters (S-107) and PFAS in Food Packaging (S-110).
- **Slitt** served as a peer reviewer of U.S. EPA's draft document, Draft Human Health Toxicity Assessment for Hexafluoropropylene Oxide (HFPO) Dimer Acid and Its Ammonium Salt (CASRN 13252-13-6 and CASRN 62037-80-3) Also Known as "GenX Chemicals" for Eastern Research Group
- **Slitt** served on NIH and VA review panels for the following: ES-18-007: Virtual Consortium for Translational/Transdisciplinary Environmental Research (ViCTER); 2021/01 ZRG1 GGG-Z (02) M - Member Conflict: Genes, Genomes, and Genetics Gastroenterology; and VA Merit Award Review, 2021/01 Council ZRD1 GAST-L 01 2, 12/03/2020.

COVID-19 Adaptations

Methodologies developed in the Slitt Lab with STEEP support were applied to the COVID-19 pandemic. Dr. Slitt and her laboratory partnered with Biotechne and Thermofisher Scientific to develop an inexpensive, sensitive saliva-based Sars-CoV-2 nucleic acid test. Her research group assisted Dr. Margi Teasdale and the Ram Lab to conduct a clinical research study that included >1200 paired saliva-nasal swab specimens from URI students. Results from the study showed that the test was >99% accurate, with a limit of detection of ~4000 copies of virus/ml saliva. URI is now working with commercial partners to seek FDA EUA status.

Trainee Emily Kaye prepares mouse liver samples for analysis. Photo: Emily Kaye.

Trainee Sadegh Modaresi prepares samples for analysis. Photo: Sadegh Modaresi.

Project 4: Detection Tools

Environmental Engineering: Develop passive samplers for the detection and bioaccumulation of PFAS in water and porewater

CENTRAL HYPOTHESIS:

Passive sampling can be used to detect PFAS and their precursors in air, water, and porewater.

Lead: **Rainer Lohmann,** Graduate School of Oceanography, University of Rhode Island (GSO)

Key Personnel: **Laurel Schaider,** Silent Spring Institute (SSI)

"Everest is treasured very highly as a unique monument for the globe...We say, 'Take nothing but pictures, leave nothing but footprints,' but we leave chemicals."

–Rainer Lohmann, *Washington Post*

OVERVIEW

This project is developing, validating, and deploying novel passive samplers for the detection of poly- and perfluoroalkyl substances (PFAS) in air, water, and porewater (water in the sediment) and as a potential screening tool for bioaccumulation. At contaminated sites, as the extent of a PFAS plume is investigated, the benefits of field-validated passive sampling approaches include ease of handling, shipping, and analysis; reduced potential for contamination; and lower detection limits that will be needed as regulatory agencies adjust their references doses.

This project is:

- Developing a porewater fiber for measuring PFAS concentrations.
- Collaborating with U.S. Environmental Protection Agency (EPA) to determine PFAS accumulation in bivalves (e.g., mussels and oysters), and comparing these results to the novel passive samplers.
- Validating PFAS passive sampling tools.

Sites for field validation and application are located on Cape Cod, MA, including in ponds near Joint Base Cape Cod, where groundwater is contaminated by aqueous film-forming foams (AFFF). Researchers are engaging residents and stakeholders to address concerns about long-range PFAS transport and characterizing the extent of impacted ponds, creeks, and estuaries.

Angela Slitt (P3), Naomi Pajarillo (undergraduate mentee), and Juliana Agudelo (trainee) prepare solutions for a pharmacokinetic study on mice. Photo: Emily Kaye.

Progress to date

- Assessed the distribution of legacy and emerging PFAS in different bird tissues from coastal and offshore seabirds from the US East Coast in collaboration with U.S. EPA (Anna Robuck, trainee alumna).
- Collaborated with Brown University (Dr. Robert Hurt) on testing and modifying nanographites as potential sampling tools for PFAS (Jitka Becanova, trainee).
- Validated polyethylene sheets to detect precursor PFAS indoors and assessed indoor exposure for children (Maya Morales McDevitt, trainee alumna).
- Performed the first laboratory experiments on how to sample PFAS with thin fibers, and first tests linked to measuring the bioavailability of PFAS in controlled lab experiments in collaboration with EPA (Jitka Becanova, trainee).
- Used passive sampling tubes to derive transport and fate of PFAS in Narragansett Bay and two local wastewater treatment plants to derive sampling rates (Christine Gardiner, trainee alumna).

Plans for the final duration of the current award

- Field-test passive samplers for PFAS in a stream on Cape Cod next to a USGS gage to evaluate their performance under a range of field conditions (Matt Dunn, trainee).
- Continue field-testing passive samplers on Guam to identify PFAS sources to groundwater. (Jitka Becanova, trainee).
- Derive bioaccumulation of PFAS in mobile lab experiments relative to passive samplers. (Izak Hill, trainee and Alan Vajda).
- Validate PE sheets as outdoor air passive samplers in a waste water treatment plant in collaboration with the Narragansett Bay Commission. (Melissa Woodward, trainee).
- Test PE-tubes and PUF disks as PFAS samplers in ambient air. (Melissa Woodward, trainee).
- Assess novel PFAS in the Delaware River combining fish, water, and passive samplers. (Anna Robuck, trainee alumna).
- Participate in planning for the pending STEEP continuation.

Thomas Garrow (Lohmann Lab) and STEEP trainee Melissa Woodward hang sampling bowls at a wastewater treatment plant. Photo: Maya Morales-McDevitt

Trainee Matt Dunn collects samples from the Pawcatuck River. Photo: Lohmann Lab.

PROJECT 4 TRAINEES

Jitka Becanova, Postdoctoral Researcher, GSO URI
Matt Dunn, PhD Student, GSO URI
Izak Hill, MS student, GSO URI
Melissa Woodward, PhD Student, GSO URI
Tatyana Yanishevsky, MS Student, GSO URI
Asta Zerue Habtemichael, PhD Student, GSO URI

PROJECT 4 GRADUATES

Erik Dixon-Anderson, MS, GSO URI, 2019; Scientist, Tris Pharma
Christine Gardiner, MS, GSO URI, 2021; URI Coastal Institute, RTC Team
Maya Morales-McDevitt, MS, GSO URI, 2021; ORISE Fellow, US Environmental Protection Agency
Anna Robuck, PhD, GSO URI, 2020; Postdoctoral Fellow, Mount Sinai

PROJECT 4 SELECTED ACCOMPLISHMENTS

Manuscripts

I.T. Cousins, G. Goldenman, D. Herzke, A.B. Lindstrom, **R. Lohmann**, M. Miller, C.A. Ng, S. Patton, M. Scheringer, X. Trier, L. Vierke, Z. Wang, J.C. DeWitt. 2019. The concept of essential use for determining when uses of PFASs can be phased out. *Environ Sci: Process Impacts*, 21(11):1803-1815. doi: 10.1039/c9em00163h. ***Selected as one of the Best Papers of 2019***

A. Cordner, V.Y. De La Rosa, **L.A. Schaider**, R.A. Rudel, L. Richter, P. Brown. 2019. Guideline levels for PFOA and PFOS in drinking water: the role of scientific uncertainty, risk assessment decisions, and social factors. *J Exp Sci Environ Epidemiol*, 29,157-171. doi: 10.1038/s41370-018-0099-9. ***2020 ISES Award for Best JESEE Paper***

A.R. Robuck, M.G. Cantwell, J. McCord, L. Addison, **M. Pfohl**, M.J. Strynar, R. McKinney, D.R. Katz, D.N. Wiley, **R. Lohmann**. 2020. Per- and Polyfluoroalkyl Substances (PFAS) in Juvenile Seabirds from the US Atlantic Coast. *Environ Sci Technol*, 54, 20, 12938-12948.

R. Lohmann, I.T. Cousins, J.C. DeWitt, J. Glüge, G. Goldenman, D. Herzke, A.B. Lindstrom, M. Miller, C.A. Ng, S. Patton, M. Scheringer, X. Trier, L. Vierke, Z. Wang. 2020. Are fluoropolymers really polymers of low concern and separate from other PFAS? *Environ Sci Technol*, 54, 20, 12820-12828 10.1021/acs.est.0c03244

J. Glüge, M. Scheringer, I.T. Cousins, G. Goldenman, D. Herzke, A.B. Lindstrom, **R. Lohmann**, M. Miller, C.A. Ng, S. Patton, X. Trier, Z. Wang, J.C. DeWitt. 2020. What are PFAS used for? An overview of the applications of per- and polyfluoroalkyl substances (PFAS). *Environ Sci: Process Impacts*, 22, 2345–2373.

I.T. Cousins, J.C. DeWitt, **R. Lohmann**, J. Glüge, G. Goldenman, D. Herzke, M. Miller, C.A. Ng, M. Scheringer, Z. Wang. 2020. The High Persistence of PFAS is Sufficient for their Management as a Chemical Class. *Environ Sci: Process Impacts*, 22(12), pp. 2307–2312. DOI:10.1039/D0EM00355G.

I.T. Cousins, J. Glüge, G. Goldenman, D. Herzke, **R. Lohmann**, C. Ng, M. Scheringer, Z. Wang. 2021. FINDING ESSENTIALITY FEASIBLE – answers to common questions concerning the "essential use" concept. *Environ Sci: Process Impacts, accepted*.

Trainee Matt Dunn collects samples from the Pawcatuck River. Photos this page: Michael Salerno.

A.R. Robuck, J. McCord, M.J. Strynar, M.G. Cantwell, D.N. Wiley, **R. Lohmann**. 2021. Tissue-specific distribution of legacy and novel per- and polyfluoroalkyl substances in juvenile seabirds. *Environ Sci Technol Lett*, 8, 457−462 https://doi.org/10.1021/acs.estlett.1c00222

J. Becanova, Z. Saleeba, A. Stone, R.H. Hurt, **A. Robuck**, **R. Lohmann.** 2021. A graphene-based hydrogel monolith with tailored surface chemistry for PFAS passive sampling. *Environ Sci Nano, accepted.*

N. Hill, **J. Becanova**, **R. Lohmann.** 2021. Development of a more sensitive method for the detection of per- and polyfluorinated compounds in dairy milk. *Anal Bioanal Chem, accepted.*

Presentations

Jamie DeWitt and **Rainer Lohmann**, "The Concept of Essential uses of PFASs," Science Response Network webinar. September 2019.

Anna Robuck and **Rainer Lohmann** When phasing out is not enough - the problem with fluorinated chemicals in wildlife. (Op-Ed) *The Hill* Oct 2020.

Rainer Lohmann et al.: Are fluoropolymers really of low concern for human and environmental health and separate from other PFAS? Chemical Watch PFAS Update, June 23, 2021.

Rainer Lohmann PFAS - from fluoropolymers to the Arctic Ocean. Thematic Webinar on PFASs French Fluorine Network (GIS), March, 16th 2021.

Rainer Lohmann et al.: Are fluoropolymers really of low concern for human and environmental health and separate from other PFAS? Collaborative on Health and the Environment. Webinar, December 3, 2020.

Laurel Schaider. PFAS and other contaminants of emerging concern in the waters of Cape Cod: Understanding exposures and addressing community concerns. Dartmouth College/ Hitchcock Medical, Department of Epidemiology, invited seminar. September 2019.

Laurel Schaider and Phil Brown. Working with communities to understand and address PFAS exposures. NIEHS Partnerships for Environmental Public Health. March 2020. https://www.niehs.nih.gov/research/supported/translational/peph/webinars/pfas/index.cfm

Laurel Schaider. PFAS effects on the immune system: What do we know and what are the links to COVID? Massachusetts Breast Cancer Coalition webinar. October 20, 2020.

Laurel Schaider. Silent Spring Institute PFAS water quality and health research. Testimony to Massachusetts PFAS Task Force, invited presentation. July 2021.

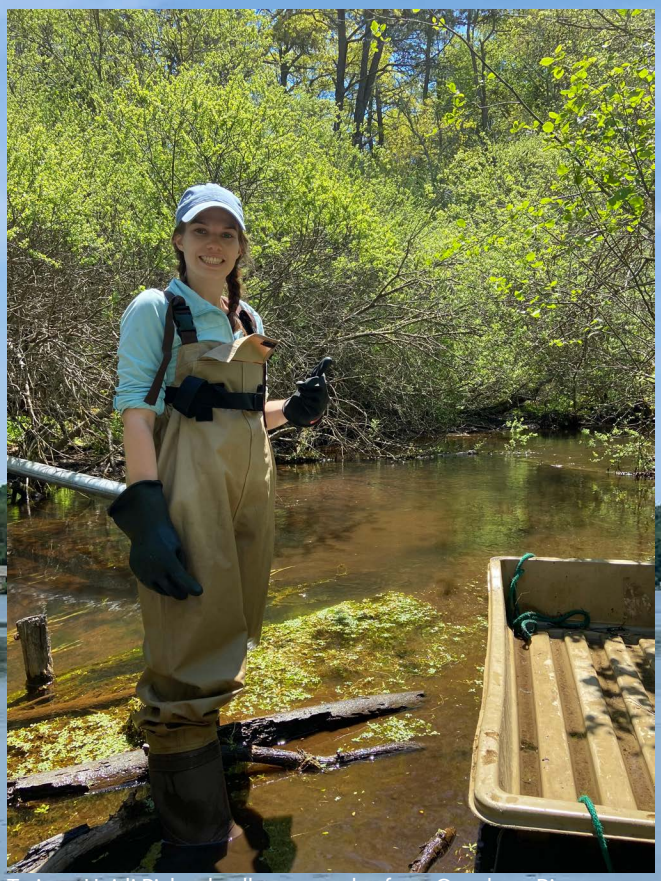
Other Activities

Rainer Lohmann appointed to RI Dept of Health's PFAS Drinking Water Technical Advisory Group.

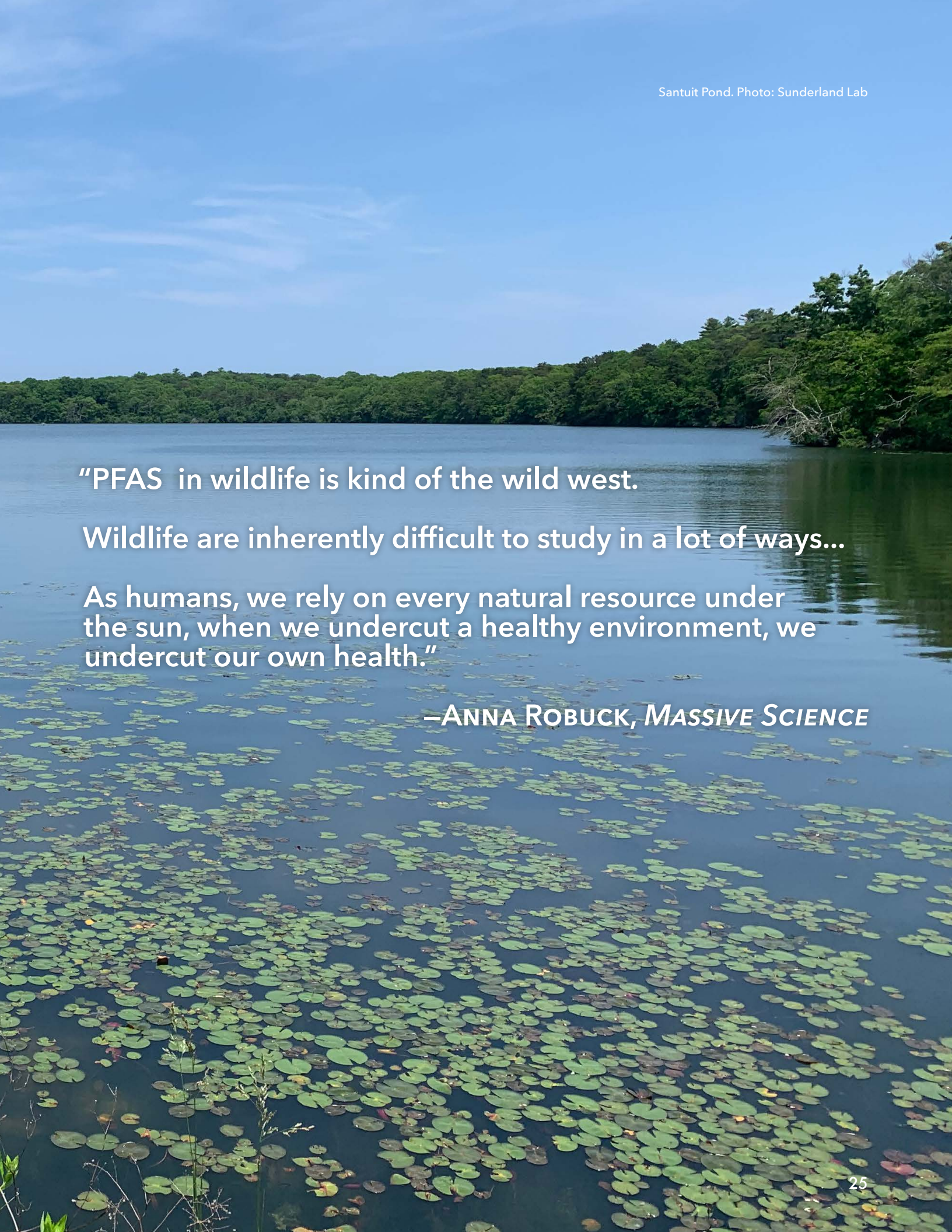
Laurel Schaider appointed to Massachusetts Department of Environmental Protection (MassDEP) technical workgroup to advise on development of screening levels for land application of PFAS in wastewater residuals.

Co-Chair with Isabel Escobar (U Kentucky), Orlando Coronell (UNC), **Rainer Lohmann** (URI), Slawo Lomnicki (LSU) and Angela Gutierrez (UK): Innovation in Remediation Strategies and their Impact on Superfund Contaminants, ACS Annual meeting, virtual April 2021.

Rainer Lohmann awarded Fulbright Fellowship as part of the Fulbright Arctic Initiative; with a research stay at the Faroe Islands Hospital System, Faroe Islands.



Trainee Heidi Pickard collects samples from Quashnet River.
Photo: Sunderland Lab.



Santuit Pond. Photo: Sunderland Lab

"PFAS in wildlife is kind of the wild west.

Wildlife are inherently difficult to study in a lot of ways...

As humans, we rely on every natural resource under the sun, when we undercut a healthy environment, we undercut our own health."

—Anna Robuck, *Massive Science*

Administrative Core

Director: **Rainer Lohmann,** Graduate School of Oceanography, University of Rhode Island (GSO)

Co-director: **Philippe Grandjean,** Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)

Project Coordinator: **Wendy Lucht,** Graduate School of Oceanography, University of Rhode Island (GSO)

OVERVIEW

As the central hub of STEEP, the Administrative Core (AC) is responsible for oversight and management of the Superfund Research Program (SRP). Its main role is to ensure the efficacy of STEEP's activities, which include producing integrated research, communicating findings to a wide range of audiences, engaging multiple researchers and communities, and training next generation scientists. The AC provides fiscal oversight and is integrated with the rest of the SRP through the director's and co-director's leadership as well as their roles in active STEEP project research, communication, and outreach. The AC, supported by the coordinator, works closely with the STEEP Internal Advisory Committee (IAC), and the External Advisory Committee (EAC).

STEEP has engaged Harrison Dekker (URI Library) to enhance data sharing within the SRP and to promote data integration among projects and cores. With support from Yana Hrytsenko, a trainee working towards her PhD in Computer Science, Dekker has been managing and curating data to move it towards the Open Science Platform while respecting the need to protect the privacy of human data. Dekker has been assisting the STEEP team in adopting fundamental FAIR data practices: data management, code management, project organization and communication. Data sharing will support public-domain release of STEEP chemical and biological data and integrated analysis with nationally available chemical and biological databases.

This core:

- Ensures successful integration of research projects and cores through regular meetings and evaluations from internal and external advisory committees.
- Provides relevant operational insights and tools for stakeholders and communities.
- Coordinates the SRP's timely response to opportunities, challenges, and evaluations.

"There's a lot that we know from science and a lot of that we don't know.

In both PFAS and coronavirus there is a lot of evidence that shows people should take precautionary measures."

—Laurel Schaider, *Cape Cod Times*

Completed and ongoing activities

- Administer the grant and subcontracts serving as the liaison between the University of Rhode Island, Harvard T.H. Chan School of Public Health, Silent Spring Institute, and the National Institute of Environmental Health Sciences (NIEHS).
- Provide financial oversight and support to each project and core.
- Manage reporting to NIEHS: Research Performance Progress Report (RPPR), Annual Update, fiscal reporting, and SRP Data Collection Tool.
- Manage the STEEP team calendar.
- Coordinate STEEP-wide interaction with federal and state agencies and stakeholders; support AC leads in maintaining comprehensive interactions with national and international leaders in the field.

HIGHLIGHTS FROM STEEP LEADERSHIP

- Rainer Lohmann appointed to U.S. EPA's Board of Scientific Counselors.
- Rainer Lohmann, Angela Slitt, and Alyson McCann appointed to the RI taskforce on setting MCLs for PFAS.
- Elsie Sunderland, Laurel Schaider and Rainer Lohmann provided expert testimony to MA PFAS Interagency Taskforce in 2021.
- Submission and administration of supplemental SRP grants linked to Data Science, Alzheimer's research, trainee externships, enhancement of diversity within health sciences, and new instrumentation.
- Supported PFAS in Our World (virtual trainee symposium), October 2020
- Preparation in progress for FLUOROS Global 2021 symposium (live site Providence, RI, and hybrid live and virtual sites in Europe, Canada, Australia, and China).
- Lead planning for pending STEEP continuation.
- Elsie Sunderland and Laurel Schaider serve on the National Academies of Sciences, Engineering and Medicine Committee on Federal Government Human Health PFAS Research.
- Philippe Grandjean appointed as reviewer for ASTDR study protocol on adverse health effects of PFAS exposure.

CONTRIBUTIONS TO PEER SRPS

- Co-organized 2nd National PFAS conference, Northeastern University, May 2019.
- Co-organize 3rd National PFAS conference in NC, 2022.
- Planned administrators' session at National SRP meeting, virtually with Texas A&M, November 2020.
- Co-hosted #PFASComm with North Carolina State University, June 2021.
- Corresponds with RI Congressional Delegation regarding NIEHS budget and PFAS-related language under consideration in federal legislation.

National and International Collaborations

SRP lead Lohmann and co-lead Grandjean continue to engage in high-level meetings at both the national and international level as well as meeting with Congressional staff. This provides STEEP with an important voice in the international emerging contaminants community, most specifically with regard to PFAS and next generation chemicals. Their work also ensures that STEEP is on the cutting edge of discovery and subsequent regulatory action.

- Grandjean continues to advise on water pollution problems in New Hampshire, Vermont, Alabama, and Michigan.
- Lohmann, as a member of the Global PFAS Science Panel, co-authored "The concept of essential use for determining when uses of PFAS can be phased out" (Cousins et al., 2019), "Are fluoropolymers really polymers of low concern and separate from other PFAS?" (Lohmann et al., 2020), and "What are PFAS used for? An overview of the applications of per- and polyfluoroalkyl substances (PFAS)" (Glüge et al., 2020). These papers have been broadly disseminated and inform policy on PFAS, particularly in the EU.
- Grandjean served as ad hoc expert on the risks to human health from PFAS-contaminated food to the European Food Safety Authority.
- Lohmann provided expert testimony to the Maine Environment and Natural Resources Committee on "Essential Use of PFAS" in May 2021.
- Grandjean has been invited to testify as a medical expert regarding PFAS pollution in Italy.

Internal Advisory Committee (IAC)

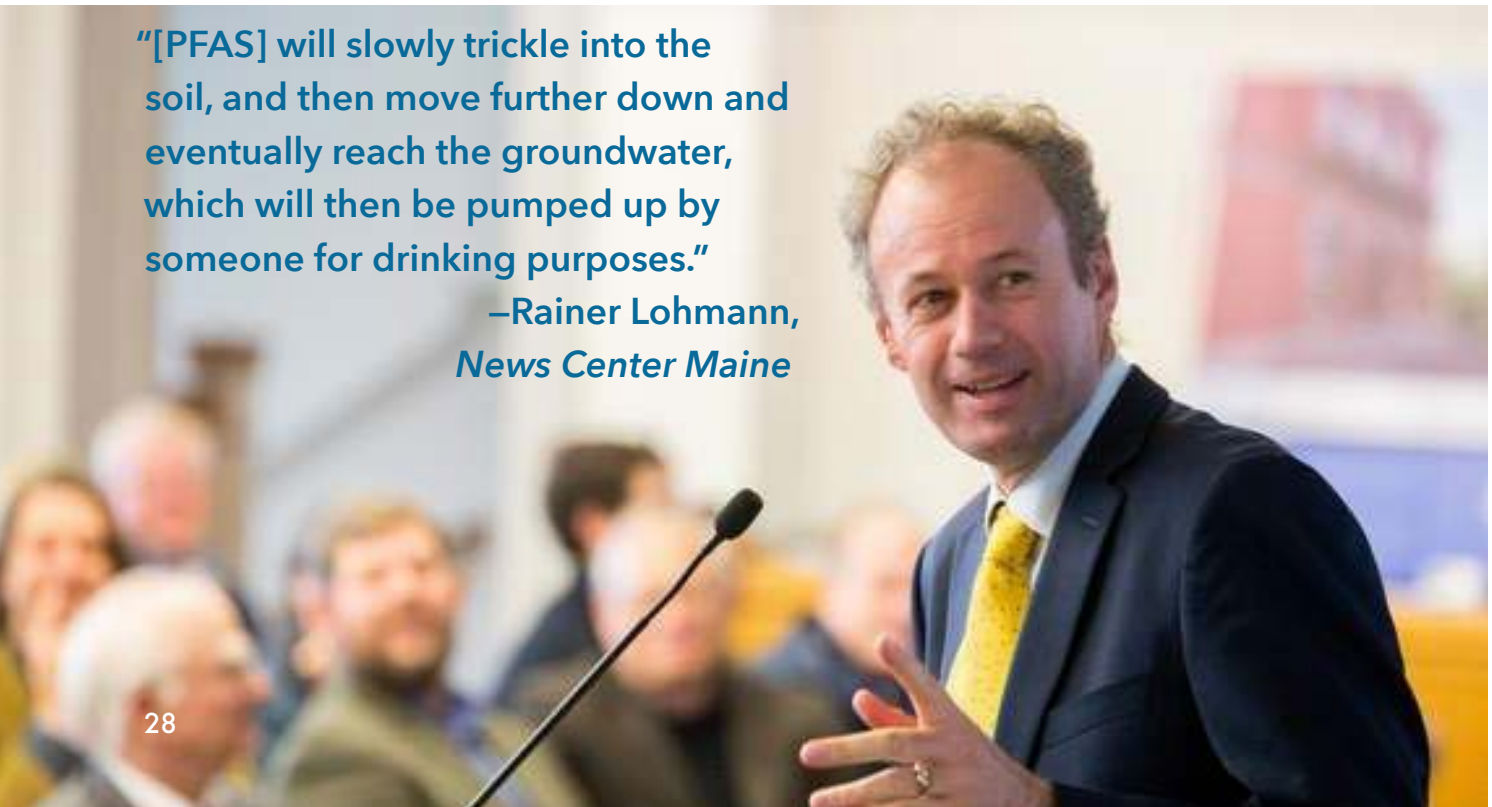
- Rainer Lohmann, PhD, SRP Director, University of Rhode Island (ex officio)
- Philippe Grandjean, MD, DMSc, SRP Co-Director, Harvard University
- Judith Swift, MA, Research Translation Core, Coastal Institute, University of Rhode Island
- Peter Snyder, PhD, Vice-President for Research and Economic Development, University of Rhode Island (ex officio)
- Art Gold, PhD, Natural Resource Sciences, University of Rhode Island
- Bongsup Cho, PhD, Pharmacy, University of Rhode Island
- Wendy Lucht, MPA, GSO, University of Rhode Island (ex officio)

The STEEP SRP reports to Vice President Snyder, and fosters the interaction of STEEP with new colleagues within URI, including the URI Health Collaborative, the URI College of Business Textiles, Fashion, and Design Department, URI Harrington School of Communication and Media, the URI College of Pharmacy, the URI College of Engineering, the URI College of Arts and Sciences, the URI College of the Environment and Life Sciences, URI Business Engagement Center, and Library Services.

External Advisory Committee (EAC)

- David Sherr, PhD, Professor Environmental Health, Boston University (chair)
- Linda Abriola, PhD, Professor, Civil and Environmental Engineering, Tufts University
- Jane Crowley, RS, MS, Eastham Health Agent, Director of Health and Environment
- Gary Ginsberg, PhD, New York State Department of Health, Director, Center for Environmental Health
- Marc A. Mills, PhD, United States Environmental Protection Agency, Office of Research and Development

The primary goals of the EAC are to provide guidance, feedback, and resources to STEEP with a focus on the scientific merit of the research; the relevance and importance of the individual components to the goals of the SRP; the integration of research across disciplines; the effectiveness of research translation activities in linking projects and stakeholders; and the appropriateness of community engagement and training activities. STEEP year 3 evaluation will take place at the EAC meeting in September 2021.



Research Translation Core

Core Lead: **Judith Swift,**
Coastal Institute at URI

Co-lead: **Amber Neville,**
Coastal Institute at URI

Co-lead: **Nathan Vinhateiro,**
Coastal Institute at URI

RTC and CEC collaborate on STEEP "Let's Talk About PFAS" public webinar series.

OVERVIEW

The Research Translation Core (RTC) continues to make STEEP's research results and the implications of these findings readily accessible to stakeholders to assist them in understanding the effects and characterizing the risk of PFAS exposure. As part of this iterative communication strategy, RTC embeds opportunities for stakeholders to provide feedback to SRP researchers at regular intervals, complemented by a clear timeline for researchers to provide updates in response to community concerns. As this process continues, stakeholders and researchers continue to narrow in on scientific questions and research strategies that are essential to management and regulatory applications as well as supporting an informed community. During the period of this report, several planned interactive focus groups were postponed due to COVID-19.

To accomplish overarching bidirectional communication, RTC develops targeted messages for: 1) researchers within STEEP and the broader SRP network; 2) state and federal agencies including the NIEHS, U.S. EPA, Agency for Toxic Substances and Disease Registry (ATSDR), and Tribal Councils; 3) other end-users with a focus on communities on Cape Cod, MA, and the Faroe Islands; and 4) additional groups as identified or, in turn, reach out to STEEP.

This core:

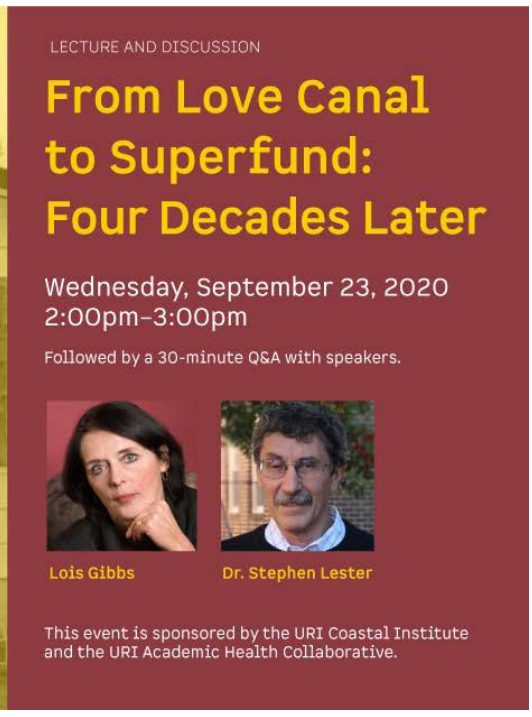
- Ensures STEEP's results are widely disseminated guided by principles of the Transtheoretical Model of behavior change (TTM).
- Provides information to state and federal regulators as well as industry leaders to influence the mitigation of PFAS use to protect human and environmental health.
- Facilitates technology transfer where appropriate.
- Synergizes relationship with Community Engagement Core (CEC) to ensure wide dissemination of information to affected communities, and improve communication techniques of STEEP trainees, scientists, and researchers.
- Coordinates broad-spectrum outreach and communication efforts in partnership with CEC and Training Core (TC).

RTC is adapting the message complexity to suit individual target audiences without jeopardizing the scientific rigor demanded by the investigation of emerging contaminants.

Progress to date

- Continued to consistently update website—www.uri.edu/steep—including conceptual design of infographics, illustrations, and mixed-use communication tools to stimulate intellectual and emotional response to engage affected communities. Continue to use social media as a means to drive Gen Zs and millennials to the website.
- In the process of producing short videos (mini-vids) of an online guide who will assist website users to explore the site with enrichment assistance much like voiced guides in a museum.
- Developing medical tip sheets for patient use in waiting areas of primary care physicians and pediatricians in addition to more detailed guidelines for physician assistance and awareness.
- Continued to enhance STEEP branding and promote PFAS science education through social media.
- Presented RTC/CEC workshop on monthly NIEHS webinar to provide training in the use of roleplay to enhance efficacy of information exchange with diverse groups in community settings.
- Published tri-annual STEEP newsletter: https://web.uri.edu/steep/news-events/newsletter/
- Continue to develop library of outreach resource material: https://web.uri.edu/steep/resources/
- Continued to provide one-on-one virtual coaching for trainees and research faculty (testifying in formal bodies, promoting events, engaging with the public, utilizing social media, informing elected officials, applying for awards, fellowships, etc.).
- Developed and launched "PFAS in Our World," (October 2020) conference website, created related promotional graphics and published conference presentation for public consumption: https://web.uri.edu/steep/save-the-date-october-13-14-2020-pfas-in-our-world-what-we-know-and-what-we-can-do/
- Presented a virtual webinar, "From Love Canal to Superfund (September 23, 2020)," featuring "homemaker to hell-raiser" Lois Gibbs and her colleague Dr. Stephen Lester to discuss the battle that led to the creation of the EPA's Comprehensive Environmental Response, Compensation, and Liability Act aka Superfund.
- In collaboration with CEC, helped plan and promote the "Let's Talk About PFAS" webinar series, focusing on topics including clean drinking water, public health, essential use, and detection of contamination. Presentations and video of the series available at: https://web.uri.edu/steep/join-steep-scientists-for-the-lets-talk-about-pfas-webinar-series/

An abandoned home near Love Canal in Niagra Falls. (UPI Photo)



- Created FLUOROS Global 2021 (October 2021) website and promoted via social media using DEI materials to diversify attendees and developed symposium materials including program guide, posters, and postcards: https://web.uri.edu/steep/welcome-to-fluoros-global-2021/
- Advertised FLUOROS 2021 via press release, interviews, e-mail marketing, listservs, on-line calendars, and social media.
- Developed template for CEC on town specific testing results and updated the well-water findings factsheet: https://web.uri.edu/steep/files/Cape-Cod-Wells-02.pdf
- Participated in STEEP renewal development and submission, including editing, layout, diagram creation, and assistance with overall assembly.

- Provided two-sided one-pager to address concerns regarding contamination of local Rhode Island plastics plant: https://web.uri.edu/steep/assessment-of-pfas-contamination-from-a-local-plastics-plant-in-narragansett-ri/
- Produced annual update for key stakeholders and administrators: https://web.uri.edu/steep/steep-aims-renewed-commitment-for-the-public-good-fall-2020-progress/

Plans for the final duration of the current award

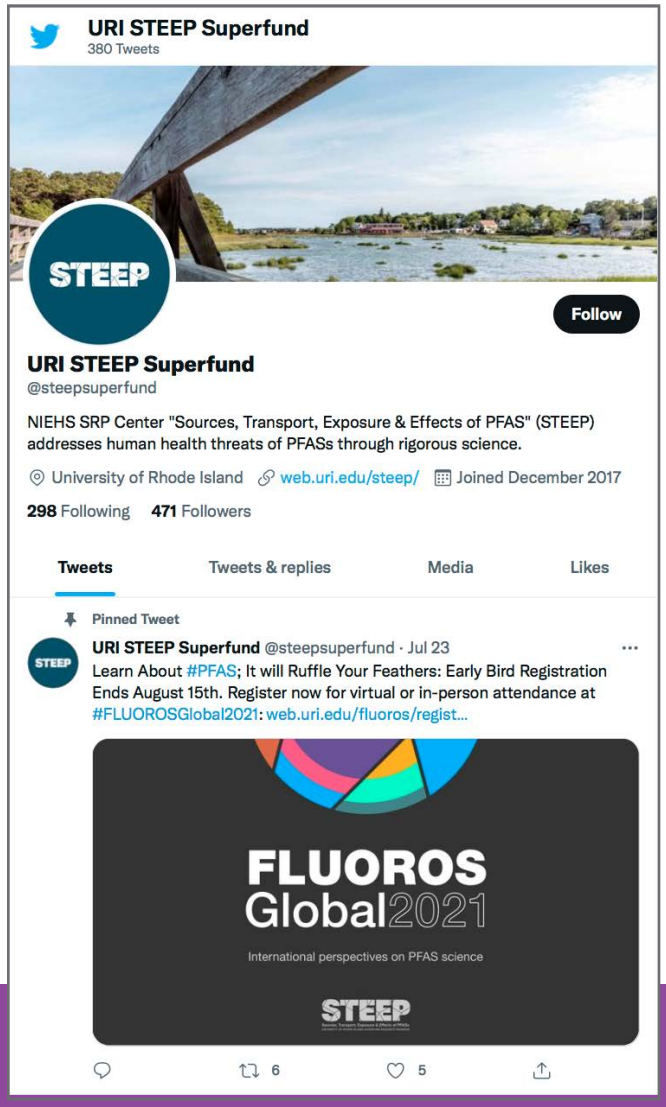
- Complete tip cards on continued use versus disposal of PFAS-laden products, medical monitoring, and adverse health effects of PFAS exposure. *CI—2021
- Create one-pager for healthcare providers and tip cards for medical waiting rooms focused on ubiquitous and toxic nature of PFAS and potential for long-term—but slow developing—adverse health impacts. *CI—2021
- Continue revision of current website to capture accomplishments and additional goals. New features (pop-up videos and podcasts) to assist the public in navigating the complexity of information. Evolving values will reflect DEI. *CI—2021
- Develop additional videos, promote through social media, and make viewable on both the STEEP website and YouTube.
- Complete development of six 10-minute PFAS-focused podcasts, e.g., history, health risks, regulation and remediation, consumer products, and disposal/phaseout strategies. *CI—2021
- Continue work with CEC to promote current efforts and, as possible, RTC will develop additional programming to reach target groups with specific interests and concerns.
- Seek funding to support translation of tip cards and information sheets to Spanish, et al.
- Develop informational 2-pager on COVID-19 and PFAS and their link due to chemicals' immune system adverse health impacts.
- Host STEEP exhibit at Graduate School of Oceanography Science Saturday, providing resources and interactive materials to the public.

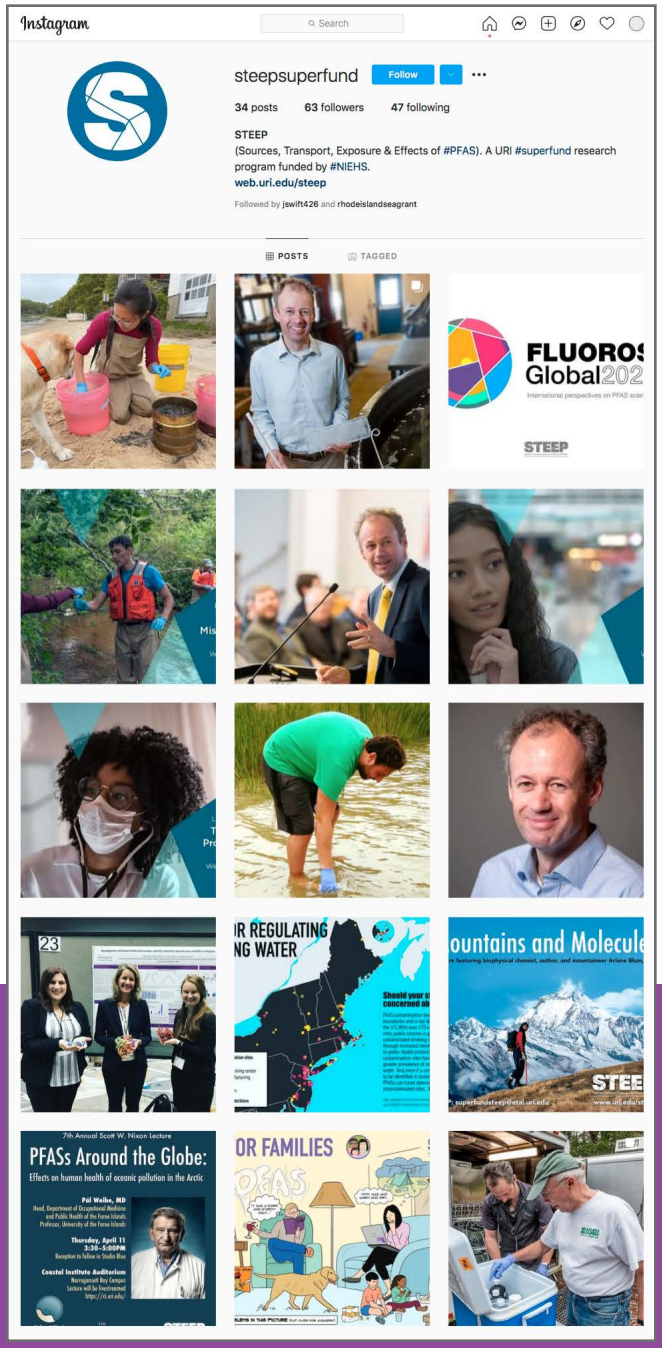
RESEARCH TRAINING CORE SELECTED ACCOMPLISHMENTS

FLUOROS 2021 Symposium website: https://web.uri.edu/fluoros/

PFAS in Our World Presentations on YouTube: https://www.youtube.com/playlist?list=PL7Foe0lm6aewhX9Nn_hMFVgzQvWnDgreu

- STEEP "Let's Talk About PFAS: webinar series: https://web.uri.edu/steep/join-steep-scientists-for-the-lets-talk-about-pfas-webinar-series/
- STEEP Aims: Renewed Commitment for the Public Good (STEEP Annual Report 2020) https://web.uri.edu/steep/steep-aims-renewed-commitment-for-the-public-good-fall-2020-progress/
- Promotion of FLUOROS 2021 and dissemination of symposium presentations and white paper via STEEP network.
- Participate in planning for the pending STEEP continuation.





Social media outreach

Twitter Stats:
7K impressions in last quarter

Learn About PFAS; It will Ruffle Your Feathers! Early Bird Registration Open for FLUOROS 20201!
2404 Impressions, 54 engagements

STEEP Dir. Dr. Rainer Lohmann will discuss essential and non-essential uses of #PFAS in consumer products. From dental floss & cosmetics to medical implants & take-out containers, we'll explore the many uses and alternatives to their use
3,040 impressions, 91 engagements

STEEP scientists discuss efforts to track down harmful #PFAS chemicals in the environment, including large quantities of previously undetected PFAS in #CapeCod.
2190 Impressions, 40 engagements

Community Engagement Core

Co-lead: **Alyson McCann,** College of the Environment and Life Sciences, University of Rhode Island (CELS)

Co-lead: **Laurel Schaider,** Silent Spring Institute (SSI)

Senior Investigator: **Emily Diamond,** Communication Studies/Marine Affairs, University of Rhode Island

Edwina Graham of the Mashpee Wampanoag Tribe on Cape Cod.

OVERVIEW

Community Engagement Core (CEC) activities are centered on Cape Cod, MA, a region where groundwater and drinking water have been impacted by per- and polyfluoroalkyl substances (PFAS). The CEC is engaging with residents, local officials, non-profit organizations, and regulators to protect human health and support local water quality protection.

This core is:

- Implementing a PFAS testing and report-back program for private well owners on Cape Cod.
- Hosting an annual STEEP Science Day on Cape Cod for researchers and trainees to share research findings and for stakeholders and community members to ask questions and inform research and engagement activities.
- Participating in community events and responding to the community's needs by providing scientific expertise in response to local questions and concerns.
- Promoting and implementing prevention and intervention strategies to reduce exposures to PFAS.

The CEC is collaborating with its core community partners, the Massachusetts Breast Cancer Coalition (MBCC) and the Sierra Club Cape Cod & Islands Group, to expand community outreach by engaging a broader base of each community partners' constituents. The CEC's activities on Cape Cod are connected to STEEP research projects. Private well testing results will inform chemical "fingerprinting" as part of the Environmental Fate & Transport research, and input from Cape residents and stakeholders will inform site selection as part of the Detection Tools research.

DATE	FEMALE	MALE	TOTAL	STEEP SAMPLED PARTICIPANTS' WELL WATER
9/14/20	3	6	9	Yes
10/8/20	4	3	7	Yes
2/16/21	7	1	8	Yes
2/24/21	1	6	7	Yes
3/9/21	4	4	8	No
3/16/21	1	3	4	No
3/17/21	6	2	8	No

Participants in private well owner focus groups

Progress to date

PRIVATE WELL STUDY AND INTERVIEWS WITH PARTICIPANTS

As part of its October 2019 Science Day, the CEC shared an overview of the preliminary findings from its Cape Cod private wells study. These findings were based on the first 101 wells from 12 towns that were sampled and summarized in a fact sheet developed in collaboration with RTC. Each participant received a customized report with the results for their own well that was developed using SSI's Digital Exposure Report-Back Interface (DERBI).

While plans to collect the next round of water samples have been on hold due to COVID-19, CEC has conducted a series of 20-minute phone interviews with participating private well owners on Cape Cod to capture their perspectives on information they received as participants in the study, particularly their interpretations of the information in their individual well reports. Participants were randomly selected and CEC included participants with and without detectable PFAS in their water sample. Thus far, 20 interviews have been conducted, and CEC is in the process of analyzing the interview transcripts. Interviewees expressed appreciation for the layers of information in their reports, which allowed them to see how their home compared to others in the study and relevant standards, and the ability to print a copy of the report and share the information with others.

FOCUS GROUPS OF PRIVATE WELL OWNERS

CEC held 7 focus groups via Zoom with private well water study volunteers to learn about motivations and barriers to testing private drinking water wells. Four groups were held with volunteers whose wells had already been tested and three groups were held with volunteers whose wells have not yet been sampled. An in-depth content analysis is being conducted on the focus groups. The resulting information will help CEC to understand what motivates private well owners on Cape Cod to test—or not—their drinking water.

PLANNING FOR SCIENCE DAY SERIES

In collaboration with RTC and the Town of Barnstable, CEC has hosted a series of four public webinars, called "Let's Talk About PFAS," featuring STEEP researchers and trainees, Cape Cod officials, and partner researchers. Each session has consisted of live presentations followed by Q&A with STEEP team members. The Town of Barnstable has hosted these presentations via Zoom. Each session has attracted well over 100 participants on Zoom, and the events were also streamed live online and re-broadcast on the local access cable channel.

- "How Can I Tell if PFAS Are in My Drinking Water?" February 3, 2021 https://web.uri.edu/steep/lets-talk-about-pfas-new-monthly-speaker-series-to-help-communities-address-contamination-and-reduce-exposures/

- "Taking Action to Protect Your Health," March 11, 2021 https://web.uri.edu/steep/march-11th-lets-talk-about-pfas-taking-action-to-protect-your-health/
- "Don't Need It, Don't Use It," April 14, 2021 https://web.uri.edu/steep/april-14-lets-talk-about-pfas-dont-need-it-dont-use-it/
- "The Case of the Missing Contaminants," June 23, 2021 https://web.uri.edu/steep/june-23-lets-talk-about-pfas-the-case-of-the-missing-contaminants/

ENGAGING WITH HIGH SCHOOL STUDENTS ON CAPE COD

Our 2019 Science Day included 80 students from five Cape Cod high schools. Building on this foundation, CEC has collaborated with the Training Core to develop a list of PFAS-centered lessons that would fit within a range of science and social science high school curricula and is partnering with the head of the Sierra Club Cape Cod Group, who is also a high school teacher, to reach teachers in biology, chemistry, and environmental science on Cape Cod.

ENGAGING WITH MASHPEE WAMPANOAG TRIBE

The CEC has formed a partnership with the Mashpee Wampanoag Tribe on Cape Cod to develop collaborations, including measuring PFAS in drinking water and fish and shellfish, evaluating whether members of the Tribe face uniquely elevated exposures due to their reliance on local resources, and developing strategies for communicating information about risks with Tribe members. Emily Diamond, who holds a joint appointment as professor of Communication Studies and Marine Affairs at URI, is leading this effort. In 2020 and 2021, engagement began by establishing and holding biweekly meetings with a tribal liaison; conducting preliminary focus groups with tribal members to understand risk perceptions, fishing and consumption behaviors, and links between natural resources and tribal identities; and sampling fish and shellfish from tribal areas to determine baseline levels of PFAS in the food supply.

CONTRIBUTING TO STATE-LEVEL DECISION-MAKING

CEC PIs have contributed to state-level decision-making processes regarding PFAS in MA and RI. McCann—along with STEEP researchers Rainer Lohmann and Angela Slitt—is a member of the RI Department of Health's PFAS Drinking Water Technical Advisory Committee and is actively providing input on the development of PFAS drinking water standards. Schaider, along with other STEEP researchers, submitted written comments to the MA Department of Environmental Protection (MassDEP) in February 2020 on proposed state drinking water standards (MCLs) and she was invited to give a presentation to the Massachusetts PFAS Task Force in July 2021. Schaider and MBCC's executive director Cheryl Osimo also provided oral testimony at a public hearing about the proposed MCLs in January 2020, and Schaider has provided testimony on scientific background for PFAS-related bills in Massachusetts, Maine, Rhode Island, and Connecticut.

COLLABORATION WITH COMMUNITY GROUPS AND ATTENDANCE AT COMMUNITY EVENTS

Prior to COVID, STEEP trainees, CEC, and RTC met with residents and distributed informational materials at community events, including:

- Cape Cod Moms Parent Resource Fair, Barnstable, MA, Jan. 25, 2020
- Local Environmental Action Conference, Boston, MA, March 7, 2020
- Rhode Island Land and Water Conservation Summit, Kingston, RI, March 7, 2020
- Barnstable County's Virtual Water Fair (moved to online), starting May 30, 2020
- Outreach activities have been curtailed due to COVID-19.

Schaider provided an update of STEEP's private well water testing program at SSI's December 2019 Cape Cod research update, attended by over 60 participants and covered by local media.

Schaider presented at a community event on November 13, 2019, hosted by the Unitarian Universalist Fellowship of Falmouth and co-hosted by the Sierra Club Cape Cod Group and MBCC.

Osimo of MBCC provided PFAS updates to the Barnstable Town Council, the Hyannis Water Board, and Greater Hyannis Civic Association. STEEP materials have been shared at community events on Cape Cod and throughout MA at tables organized by MBCC.

At the request of one of the West Barnstable Water Commissioners, Schaider provided an information session and accompanying one-page overview summarizing CEC's private wells study at commissioners' meeting in February 2020.

Schaider presented an update on SSI's PFAS research, including an overview of STEEP, at a meeting of the Barnstable County Commissioners on April 7, 2021.

Schaider presented an update on SSI's PFAS research, including an overview of STEEP, at a meeting of the Hyannis Rotary Club on June 10, 2021.

Plan for the final duration of the current award

- *Follow-up round of private well testing and report-back*. In collaboration with Projects 1 and 4, CEC aims to collect water samples from another 100 private wells on Cape Cod in August and September 2021. Members of the Mashpee Wampanoag Tribe will be especially welcomed to participate.
- *Interviews with private well study participants*. CEC will continue analyzing results from interviews with study participants for publication in a peer-reviewed journal article.
- *Focus groups with private well owners*. CEC will complete content analysis of focus groups and synthesize findings for publication in a peer-reviewed journal article.
- *Community events and Science Day*. Pending continued lifting of COVID-19 restrictions, CEC will resume hosting in-person events, such as a Science Day research update and a film screening, and begin attending in-person community events.
- *High school engagement*. CEC will continue to work with MBCC and the Sierra Club Cape Cod Group to develop webinars for high school students and engage with high school students and teachers across Cape Cod to discuss water quality and emerging contaminants.
- *Mashpee Wampanoag Tribe engagement*. Once the results of the spring 2021 shellfish sampling are received, CEC will work with RTC to translate findings into tribal-specific materials and communication strategies. CEC will also prioritize the development of a series of engagement activities to inform tribal members about PFAS risks. The results of the spring 2021 focus groups on the link between PFAS risk perceptions and tribal cultural identity will also be written up for publication in a peer-reviewed journal.
- *State-level policymaking*. McCann will continue to work on the RI Department of Health's PFAS Technical Advisory Committee and serve as a resource to this committee. Schaider will continue to provide input to MassDEP and will attend meetings of MassDEP's technical workgroup on PFAS & Residuals.
- *Meetings with Cape Cod Community Advisory Committee (CAC) and other stakeholders*. CEC will continue to meet with the Cape Cod CAC and other stakeholders to identify additional community engagement opportunities.
- Participate in planning for the pending STEEP continuation.

"We need a class-based solution that phases out nonessential uses of PFAS."

–Laurel Schaider, *Providence Journal*

COMMUNITY ENGAGEMENT CORE SELECTED ACCOMPLISHMENTS

Presentations

Schaider L., **McCann A.**, Hernandez A., **Pickard H.**, Balcom P., **Sunderland E.** Legacy and alternative PFAS compounds in private wells on Cape Cod, Massachusetts, USA. Oral presentation. Society of Environmental Toxicology and Chemistry North America 40th Annual Meeting, Toronto, 2019.

Schaider L., **McCann A.**, Hernandez A., **Pickard H.**, Balcom P., **Sunderland E.** Legacy and Alternative PFAS Compounds in Private Wells on Cape Cod, Massachusetts, USA. Poster presentation. NIEHS Superfund Research Program Annual Meeting, Seattle, 2019.

Schaider L., **McCann A.**, Hernandez A., Philo L., Osimo C. Using a digital online report-back tool (DERBI) to communicate results of PFAS testing to private well owners on Cape Cod, Massachusetts. Presentation (virtual). NIEHS Superfund Research Program Risk Communication Conference. 2021.

Webinars

"PFAS in Massachusetts Drinking Water: An Update on Research and Regulations." Laurel Schaider. Hosted by Massachusetts Breast Cancer Coalition. October 30, 2019.
https://mbcc.org/pfas-in-drinking-water-january-29-webinar/

"Working with communities to understand and address PFAS exposures." **Laurel Schaider**, Phil Brown. NIEHS Partnerships for Environmental Public Health webinar. March 24, 2020.

"PFAS effects on the immune system: What do we know and what are the links to COVID?" **Laurel Schaider**. Hosted by Massachusetts Breast Cancer Coalition monthly webinar. October 20, 2020.

"Food packaging as a source of PFAS exposure." **Laurel Schaider**. Panel discussion hosted by Massachusetts Breast Cancer Coalition. December 8, 2020.

"Let's Talk About PFAS: How Can I Tell if PFAS Are in My Drinking Water?" **Laurel Schaider**, **Alyson McCann**. Webinar series hosted by STEEP. February 3, 2021.

"PFAS: What are they and why are they a concern?" **Laurel Schaider**. Metrowest Climate Solutions PFAS Forum (Wayland, MA). June 3, 2021.

Local media coverage and editorials

Cape Cod Times, 12/11/19 (Editorial)
Written by Laurel Schaider and Cheryl Osimo. "PFAS: A local and global challenge."
https://www.capecodtimes.com/opinion/20191211/pfas-local-and-global-challenge

Cape Cod Times, 12/11/19.
"Researchers: Hyannis PFAS studies will move ahead."
https://www.capecodtimes.com/news/20191211/researchers-hyannis-pfas-studies-will-move-ahead

Barnstable Patriot, 12/12/19
"Silent Spring shares latest research on PFAS exposure"
https://www.barnstablepatriot.com/news/20191212/silent-spring-shares-latest-research-on-pfas-exposure

CapeCod.com, 12/12/19
"Silent Spring Institute Provides Updates on PFAS Studies."
https://www.capecod.com/newscenter/silent-spring-institute-provides-updates-on-pfas-studies/

Cape Cod Times, 7/12/20
"Carcinogenic chemicals found in Nantucket well water."
https://www.capecodtimes.com/story/special/special-sections/2020/07/12/carcinogenic-chemicals-found-in-nantucket-well-water/114066352/

Spectrum weekly radio program on iHeartRadio, 11/29/20
Interview with Laurel Schaider.
https://www.iheart.com/content/2020-11-24-silent-spring-institute/

CapeCod.com, 12/13/20
"Breast Cancer Coalition Addresses Dangers of PFAS Chemicals."
https://www.capecod.com/newscenter/breast-cancer-coalition-discussed-dangers-of-pfas-chemicals/

Cape Cod Times, 7/13/21
"'Forever chemicals' detected in Chatham drinking water wells."
https://www.capecodtimes.com/story/news/2021/06/23/chatham-municipal-well-shut-down-due-high-pfas-levels/5321528001/

Other media coverage and editorials

WBUR Boston, 11/8/19
"What Are PFAS Chemicals, And Should I Be Freaking Out About Them?"
https://www.wbur.org/earthwhile/2019/11/08/what-are-pfas-chemicals-and-should-i-be-freaking-out-about-them

National Geographic, 1/24/20
"Toxic 'forever chemicals' more common in tap water than thought, report says"
https://www.nationalgeographic.com/science/2020/01/pfas-contamination-safe-drinking-water-study/

Inverse, 3/2/20
"PFAS: Your home is full of potentially harmful "forever chemicals" – here's what you need to know"
https://www.inverse.com/mind-body/pfas-explained-your-home-is-full-potentially-harmful-forever-chemicals

Environmental Health News, 7/6/20
"Op-ed: PFAS chemicals–the other immune system threat"
https://www.ehn.org/pfas-and-immune-system-2646344962.html

Wired, 8/7/20
"The End Is Nearer for 'Forever Chemicals' in Food Wrappers"
https://www.wired.com/story/the-end-is-nearer-for-forever-chemicals-in-food-wrappers/

PNAS, 4/13/21
"News Feature: How "forever chemicals" might impair the immune system"
https://www.pnas.org/content/118/15/e2105018118

Boston.com, 6/3/21
"Why do so many Mass. communities have contaminated drinking water?"
https://www.boston.com/news/science/2021/06/03/massachusetts-communities-contaminated-drinking-water/

WBUR, 7/7/21
"Northeastern University Expert Recommends State Task Force Test Blood for Chemical Contaminant PFAS"
https://www.wbur.org/earthwhile/2021/07/07/northeastern-university-chemical-pfas-test-blood

Research Translation Core products displayed at Community Engagement Core public event. Photo: Michael Salerno.

Training Core: Next Generation

Co-lead: **Angela Slitt,** URI College of Pharmacy (Pharm)

Co-lead: **Elsie Sunderland,**
Harvard T.H. Chan School of Public Health, Department of Environmental Health (HSPH)
Harvard John A. Paulson School of Engineering and Applied Sciences (SEAS)

Assessment Coordinator: **John Stevenson,** Professor Emeritus of Psychology, University of Rhode Island (PSY)

TC Coordinator: **Alicia Crisalli,** PhD Student, Pharm URI, TC Trainee

OVERVIEW

The STEEP Training Core (TC) is responsible for shaping the next generation of environmental health scientists into well-rounded researchers with an interdisciplinary approach and the professional skills necessary to succeed after graduate school. The TC will provide pre- and post-doctoral level STEEP trainees with additional resources and opportunities to become skilled scientists and engineers. They will be able to address various aspects of emerging contaminants, specifically empirical research, practical remediation, community engagement, and research translation facets of PFAS.

A Sunderland Lab member collects fish for PFAS analysis.
Photo: Sunderland Lab.

Trainee Bridger Ruyle collects eels from Santuit River.
Photo: Sunderland Lab.

The primary goals of the Training Core are to:

- Promote and coordinate inter- and intra-institutional as well as interdisciplinary cross-training experiences.
- Provide professional development opportunities to enhance leadership, peer-to-peer mentoring, outreach, and communication skills.
- Collaborate with Research Translation and Community Engagement Cores to provide skills often not addressed in traditional PhD programs.
- Connect trainees through social media to create a cohesive and integrated team.
- Support intra-STEEP lab exchanges and participation in professional conferences.

The TC is capitalizing on STEEP's multi-institutional strength by focusing on innovative and interdisciplinary training activities. The TC supports three distinct groups of research trainees over the entire five-year grant cycle: fully supported pre-doctoral trainees, fully supported post-doctoral trainees, and partially STEEP-funded graduate students and post-doctoral fellows. In addition, two STEEP fellowships for students from underrepresented minority groups are being supported through the URI Graduate School Diversity Program. All graduate trainees will be fully immersed in their rigorous interdisciplinary training activities.

Progress to date

- Coordinated the virtual colloquium visit by Dr. Mark Strynar of the US EPA on January 27, 2021.
- Coordinated monthly trainee meetings to present research findings or host experts for career development.
- Hosted Dr. Christopher Lau, US EPA and Dr. Maureen Gwinn, US EPA, to present on career paths in toxicology and regulatory science in 2021.
- Coordinated and held a two-day Zoom conference on October 13-14, 2020, entitled "PFAS in Our World." Alicia Crisalli (URI Pharm) and Heidi Pickard (Harvard) were conference co-chairs, and Slitt lab trainees chaired the poster sessions.
- Held joint trainee meetings with the NCSU Center for Environmental and Health Effects of PFAS.
- Formed Trainee Action Teams to provide trainees with active engagement with PFAS science and community policy. Trainees will conduct interdisciplinary projects that have on-the-ground applications.

  — Team 1: Development of pedagogy for high school students (interface with CEC)

  —Team 2: Direct engagement with community stakeholders, including underrepresented groups and ethnic minorities (led by CEC)

  —Team 3: Science translation for a variety of interest groups (led by RTC)

  —Team 4: Policy response and support action team to support local, state and Federal regulatory activities (interface with STEEP Science PIs)

"This has huge ramifications for not only our understanding of human exposure but also for how much PFAS is discharging into the ocean and accumulating in marine life."

–Bridger Ruyle, *Harvard Gazette*

"Over the past 10-15 years we've really developed this super negative picture of what PFAS do to humans. But we've barely scratched the surface of that in wildlife… PFAS in wildlife is kind of the wild west. Wildlife are inherently difficult to study in a lot of ways."

–Anna Robuck, *The Revelator*

Trainee alumna Anna Robuck tagging a great shearwater. Photo: Lohmann Lab.

- ## Plan for the final duration of the current award

- Support and encourage trainee engagement in the STEEP Lab Rotation program.
- Focus on diversity and inclusion/social and environmental justice issues.
- Continue monthly trainee meetings and joint programming with the NCSU Center for Environmental and Health Effects of PFAS.

TRAINING CORE SELECTED ACCOMPLISHMENTS

Anna Robuck (URI, STEEP Graduate):

- Successfully defended doctoral dissertation entitled "Distribution of novel and legacy organic pollutants in seabirds from contrasting marine environments" in December 2020.
- Postdoctoral Fellowship at Mount Sinai in high-resolution mass spectrometry and metabolomics.

Juliana Agudelo (URI):

- Recipient of the URI Graduate School Dean's Diversity Fellowship, academic year 2020-2021.
- Recipient of the Perry J. Gehring Diversity Student Travel Award for the Society of Toxicology Annual Meeting in Anaheim, CA in March 2020. Invited to be the society's special guest at the Undergraduate Diversity Program dinner. Juliana was featured on the Society of Toxicology's Instagram page for this 2020 SOT Endowment Fund Award.
- Recipient of the 2020 KC Donnelly Externship Award to support an externship at the EPA where she quantified PFAS concentrations in human serum and livers.
- Featured on the URI's newspaper and university magazine for the COVID-19 assay.
- Represented STEEP as a guest career panelist for the Boston University's Peer Health Exchange Program.
- Summer intern for the U.S. Environmental Protection Agency's Center for Public Health and Environmental Assessment (CPHEA), in collaboration with the New Chemicals Division (NCD). The training will focus on science infrastructure projects supporting risk assessment activities of new industrial chemicals under the Toxic Substances Control Act (TSCA).

Bridger Ruyle (Harvard):

- Recipient of 2021 KC Connelly externship award (pending official notice) to study the disposition of 6:2 FTSA and PFAS in contemporary AFFF in exposed mice in Dr. Sue Fenton's lab at the NIEHS.
- Presented research on PFAS source fingerprinting on Cape Cod at STEEP's "Let's Talk About PFAS Webinar" on June 23, 2021.
- Publication https://pubs.acs.org/doi/10.1021/acs.est.0c07296 selected as one of NIEHS extramural papers of the month June 2021.

Maya Morales-McDevitt:

- Recipient of the James Corless Prize in Marine Chemistry via the URI Foundation.
- Completion of her Master's degree in Oceanography.
- Recipient of an ORISE EPA Fellowship to commence after the successful completion of her Master's degree.

Matthew Dunn (URI):

- Recipient of 2021 KC Connelly externship award (pending official notice) to work with Cyclopure, Inc. to study "Investigation of a novel cyclodextrin sorbent to improve integrative passive sampler uptake for PFAS".

TRAINEE GRADUATES

Erik Dixon-Anderson, MS, GSO URI (Scientist, Tris Pharma)

Michael Fedorenko, MS, URI Engineering (Project Engineer at Sustainment and Restoration Services)

Christine Gardiner, MS, GSO URI (URI Coastal Institute, RTC team)

Emily Marques (formerly Martell), URI Pharmacy (Postdoctoral Fellow at UMass Amherst with Dr. Alicia Timme-Laragy)

Maya Morales-McDevitt, MS, URI GSO (ORISE Fellow at US Environmental Protection Agency)

Aleksandra Naumann, MS, URI Engineering (Health Research Associate, Institute of Machine Tools and Production Technologies, Technische Universität Braunschweig)

Marisa Pfohl, PhD, URI Pharmacy (Postdoctoral Fellow at EPA)

Andrea Tokranov, PhD, Harvard (USGS Scientist)

Clifton Dassuncao, PhD, Harvard SEAS (Scientist at Eastern Research Group)

Xindi (Cindy) Hu, PhD, Harvard SEAS (Scientist at Mathematica Policy Research, Inc.)

Damaskini Valvi, Postdoctoral Researcher, Harvard (Assistant Professor at Mount Sinai)

Anna Robuck, PhD, GSO URI (Postdoctoral Fellow at Mount Sinai with Dr. Doug Walker)

Charlotte Wagner, PhD, Harvard University (Scientist, Energy and Environmental Modeler at Stockholm Environment Institute)

TRAINEE MILESTONES

Heidi Pickard (Harvard University), qualifying examination to be Ph.D. candidate, May 2021

Matthew Dunn (URI), passed written and oral comprehensive examination to be Ph.D. candidate, February 2021

Jessica (Orr) Alesio (URI), passed written and oral comprehensive examination to be Ph.D. candidate, December 2020

NEW TRAINEE ADDITIONS

Sangwoo Ryu, Ph.D. program in Pharmaceutical Sciences, Project 3 (Slitt)

Jarod Snook, Ph.D. program in Oceanography, Project 4 (Lohmann)

Melissa Woodward, Ph.D. program in Oceanography, Project 4 (Lohmann)

Tatyana Yanishevsky, M.S. program in Oceanography, Project 4 (Lohmann)

TRAINEE PUBLICATIONS

Pfohl M., DaSilva N.A., **Marques E.**, **Agudelo J.**, Liu C., Goedken M., **Slitt A.L.**, Seeram N.P., Ma H. 2021. Hepatoprotective and anti-inflammatory effects of a standardized pomegranate *(Punica granatum)* fruit extract in high fat diet-induced obese C57BL/6 mice. Int J Food Sci Nutr, 72:499-510. doi: 10.1080/09637486.2020.1849041. Epub 2020 Nov 18. PMID: 33203257.

Hamilton M.C., Heintz M.M., **Pfohl M.**, **Marques E.**, Ford L., **Slitt A.L.**, Baldwin W.S. 2021. Increased toxicity and retention of perflourooctane sulfonate (PFOS) in humanized CYP2B6-Transgenic mice compared to Cyp2b-null mice is relieved by a high-fat diet (HFD). *Food Chem Toxicol*. 152:112175. doi: 10.1016/j.fct.2021.112175. Epub 2021 Apr 8. PMID: 33838175; PMCID: PMC8154739.

Ruyle B.J., **Thackray C.P.**, McCord J.P., Strynar M.J., Mauge-Lewis K.A., Fenton S.E., **Sunderland E.M.** 2021. Reconstructing the composition of poly- and perfluroalkyl substances (PFAS) in contemporary aqueous film forming foams. *Environ Sci Technol Lett.* 8(1):59-65. PMID: 33628855

Ruyle B.J., **Pickard H.M.**, **LeBlanc D.R.**, **Tokranov A.K.**, **Thackray C.P.**, **Hu X.C.**, **Vecitis C.D.**, **Sunderland E.M.** 2021. Isolating the AFFF Signature in Coastal Watersheds Using Oxidizable PFAS Precursors and Unexplained Organofluorine. *Environ Sci Technol*, 55(6):3686-3695. PMID: 33667081

De Silva A.O., Armitage J.M., Bruton T.A., **Dassuncao C.**, Heiger-Bernays W., **Hu X.C.**, Kärrman A., Kelly B., Ng C., **Robuck A.**, Sun M., Webster T.F., **Sunderland E.M.** 2021. PFAS Exposure Pathways for Humans and Wildlife: A Synthesis of Current Knowledge and Key Gaps in Understanding. *Environ Toxicol Chem*, 40 (3):631-657. PMID: 33201517; PMCID: PMC7906948.

Joerss H., Xie Z., **Wagner C.C.**, von Appen W.J., **Sunderland E.M.**, Ebinghaus R. 2020. Transport of Legacy Perfluoroalkyl Substances and the Replacement Compound HFPO-DA through the Atlantic Gateway to the Arctic Ocean—Is the Arctic a Sink or a Source? *Environmental Science & Technology*, 54 (16), 9958-9967. DOI: 10.1021/acs.est.0c00228

Kwiatkowski C.F., Andrews D.Q., Birnbaum L.S., Bruton T.A., DeWitt J.C., Knappe D.R.U., Maffini M.V., Miller M.F., Pelch K.E., Reade A., Soehl A., Trier X., Venier M., **Wagner C.C.**, Wang Z., and Blum A. 2020. Scientific Basis for Managing PFAS as a Chemical Class. *Environmental Science & Technology Letters*, 7 (8), 532-543 DOI: 10.1021/acs.estlett.0c00255

Marques E., **Pfohl M.**, Auclair A., Jamwal R., Barlock B.J., Sammoura F.M., Goedken M., Akhlaghi F., **Slitt A.L.** 2020. Perfluorooctanesulfonic acid (PFOS) administration shifts the hepatic proteome and augments dietary outcomes related to hepatic steatosis in mice. *Toxicol Appl Pharmaco*, 408:115250. doi: 10.1016/j.taap.2020.115250. PMID: 32979393.

Pfohl M., Ingram L., **Marques E.**, Auclair A., Barlock B., Jamwal R., Anderson D., Cummings B.S., **Slitt A.L.** 2020. Perfluorooctanesulfonic Acid and Perfluorohexanesulfonic Acid Alter the Blood Lipidome and the Hepatic Proteome in a Murine Model of Diet-Induced Obesity. *Toxicol Sci*, 178(2):311-324. doi: 10.1093/toxsci/kfaa148. PMID: 32991729; PMCID: PMC7751193.

Pfohl M., **Marques E.**, Auclair A., Barlock B., Jamwal R., Goedken M., Akhlaghi F., **Slitt A.L.** 2021. An 'Omics Approach to Unraveling the Paradoxical Effect of Diet on Perfluorooctanesulfonic Acid (PFOS) and Perfluorononanoic Acid (PFNA)-Induced Hepatic Steatosis. *Toxicol Sci*, 180(2): 277-294. doi: 10.1093/toxsci/kfaa172. PMID: 33483757; PMCID: PMC8041463.

Fedorenko M., **Alesio J.**, Fedorenko A., **Slitt A.**, **Bothun G.D.** 2021. Dominant entropic binding of perfluoroalkyl substances (PFASs) to albumin protein revealed by 19F NMR. *Chemosphere*, 263:128083. doi: 10.1016/j.chemosphere.2020.128083. PMID: 33297081.

Robuck A.R., Cantwell M.G., McCord J.P., Addison L.M., **Pfohl M.**, Strynar M.J., McKinney R., Katz D.R., Wiley D.N., **Lohmann R.** 2020. Legacy and Novel Per- and Polyfluoroalkyl Substances in Juvenile Seabirds from the U.S. Atlantic Coast. *Environ Sci Technol*. 54(20):12938-12948. doi: 10.1021/acs.est.0c01951. Epub 2020 Oct 7. PMID: 32894676; PMCID: PMC7700771.

Salter D.M., Wei W. Nahar P.P., **Marques E.**, **Slitt A.L.** 2021. Perfluorooctanesulfonic acid (PFOS) thwarts the beneficial effects of calorie restriction and Metformin. *Toxicol Sci*, doi: 10.1093/toxsci/kfab043, PMID: 33844015.

Marques E.S., **Pfohl M.**, Wei W., Tarantola G., Ford L., Amaeze O., **Bothun G.**, and **Slitt A.L.** Replacement per- and polyfluoroalkyl substances (PFAS) are potent modulators of lipogenic and drug metabolizing gene expression signatures in primary human hepatocytes. *Environmental Science and Technology, resubmitted with revisions, August 2021*.

Tokranov A.K., LeBlanc D.R., **Pickard H.M.**, Barber L.B., **Ruyle B.J.**, Hull R.B., **Sunderland E.M.**, Vecitis C.D.. 2020. PFAS Interfacial Sorption and Precursor Persistence during Transport across Surface Water/Groundwater Boundaries. *Environmental Science and Technology*. In revision.

A puffin in the Faroe Islands has just caught its next meal.

TRAINEE PRESENTATIONS

Ruyle B.J. and **Sunderland E.M.** Reconstructing proprietary PFAS compositions in AFFF. Accepted oral presentation at upcoming SETAC North America 41st Annual Conference, Fort Worth (virtual), November 2020.

Kaye E., **Agudelo J.**, **Pfohl M.**, **Marques E.**, **Slitt A.** (2020) Developmental PFOS exposure causes changes in liver transcriptome. Late-Breaking 9: Air Pollution; PFAS; Respiratory. Society of Toxicology Annual Meeting, Anaheim, CA, March 19, 2020

Marques E., **Pfohl M.**, Wei W., Tarantola G., Ford L., Amaeze O., and **Slitt A.** (2020) Replacement Per- and Polyfluoroalkyl Substances (PFASs) Are Potent Modulators of Lipogenic and Drug Metabolizing Gene Expression Signatures in Primary Human Hepatocytes.*The Toxicologist*, 2435, Society of Toxicology Annual Meeting, March 2020

Ford L., **Marques E.**, Wei W., **Pfohl M.**, **Agudelo J.**, and **Slitt A.** (2020) Time to Treatment after Plating Impacts PFAS Induction of Gene Expression in Cryopreserved Human Hepatocytes. *The Toxicologist*, 1974, Society of Toxicology Annual Meeting, March 2020

Hamilton M.C., **Pfohl M.**, **Marques E.**, Ford L., **Slitt A.**, and Baldwin W.S. Increased Toxicity and Retention of Perflourooctane Sulfonate (PFOS) in hCYP2B6-Tg Mice Compared to Cyp2b-Null Mice Is Relieved by a High-Fat Diet. *The Toxicologist*, 2433, Society of Toxicology Annual Meeting, March 2020

Trainee Sadegh Modaresi conducting a necropsy of a mouse. Credit: Sadegh Modaresi.

Trainee Jennifer Sun collecting shellfish from Quashnet River. Photo: Sunderland Lab.

Trainees

Juliana Agudelo
PhD Student
College of Pharmacy, URI
Slitt Lab

Jessica Alesio
PhD Student
College of Engineering, URI
Bothun Lab

Jitka Becanova
Postdoctoral Researcher
Graduate School of Oceanography, URI
Lohmann Lab

Alicia Crisalli
PhD Student
College of Pharmacy, URI
Cho Lab/TC Grad Assistant

Mona Dai
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Sunderland Lab

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Bridger Ruyle
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Sangwoo Ryu
PhD Candidate
College of Pharmacy, URI
Slitt Lab

Lara Schultes
Postdoctoral Researcher
School of Engineering and Applied Sciences, Harvard
Sunderland Lab

Jarod Snook
PhD Candidate
Graduate School of Oceanography, URI;
Lohmann Lab

Jennifer Sun
PhD Student
School of Engineering and Applied Sciences, Harvard
Sunderland Lab

Melissa Woodward
PhD Candidate
Graduate School of Oceanography, URI
Lohmann Lab

Tatyana Yanishevsky
Affiliate
Graduate School of Oceanography, URI
Lohmann Lab

Trainee Heidi Pickard collects water samples from Moody Pond. Photo: Sunderland Lab.

Trainee Jennifer Sun and curious bystander sort through invertebrate samples. Photo: Sunderland Lab.

THE UNIVERSITY OF RHODE ISLAND

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH
Department of Environmental Health

SILENT SPRING INSTITUTE
Researching the Environment and Women's Health

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