Assessing the Ecological Risks of PFAS: Overview of an International Workshop

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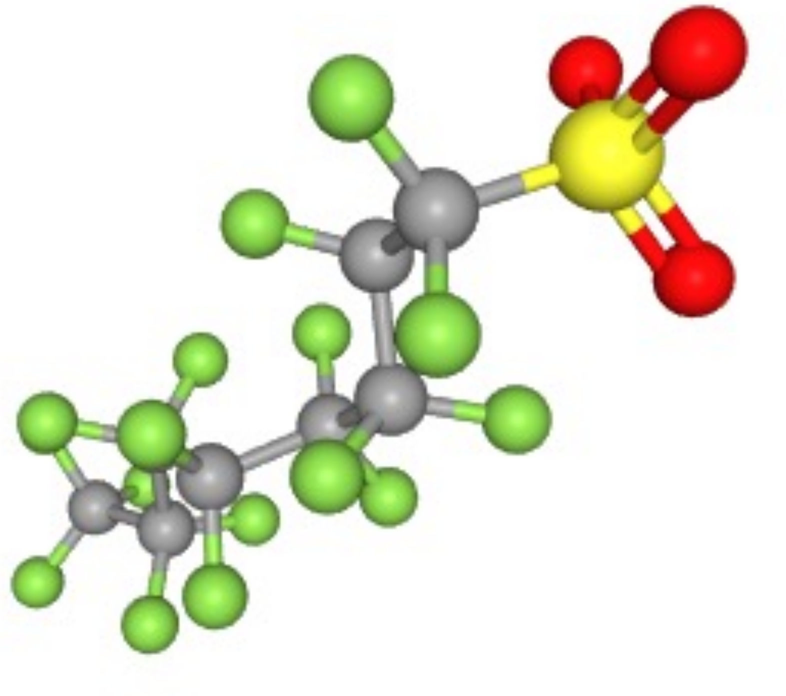
Ecological Effects of PFAS: An Emerging Emphasis

- PFAS contamination from multiple sources in aquatic and terrestrial ecosystems throughout the world

- Many PFAS in multiple structural classes, most with inadequate data to assess possible ecological occurrence/toxicity



Perfluorooctanesulfonic acid (PFOS)

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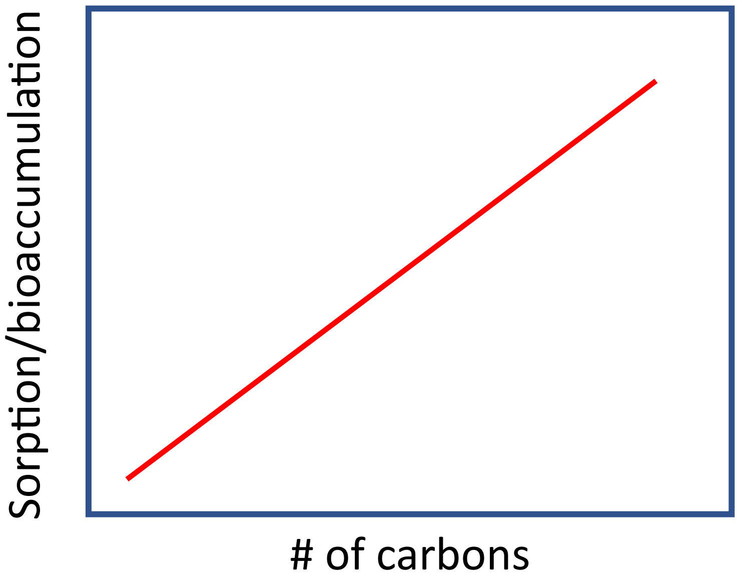
Image from NIH PubChem

Ecological Effects of PFAS: An Emerging Emphasis

- Some PFAS persistent/bioaccumulative/toxic



- Surfactant properties -> accumulation on surface of water
- PFAS extremely persistent in the environment because of strong C-F bond
  - C-F = 485 kJ/mol
  - C-Cl = 339 kJ/mol
- Transformation of precursors
- Carbon chain length and functional group affect environmental behavior

Environmental Risk Assessment of PFAS

12–15 August 2019 | Durham, NC, USA

SETAC North America Focused Topic Meeting

Four-day workshop with expert presentations and topic group breakouts/discussions

Topic groups: Analytical Chemistry; Exposure; Human Health Effects; Ecological Effects; Risk Characterization

Open forum discussions with tripartite representation—business, academia, government

https://globe.setac.org/pfas/

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(1) Background and Introduction

(2) Prioritizing for Monitoring and Testing

(3) Current Knowledge about Ecological Exposure

(4) Current Knowledge about Ecological Effects

(5) New Approach Methodology (NAM) Application to Date

(6) International Perspectives on Current ERA/Regulatory Activities

(7) Advancing Exposure Assessment

(8) Advancing Hazard Assessment

(9) Opportunities for Applying NAM

(10) Addressing the Challenge of PFAS Mixtures

(11) Conclusions and Recommendations

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Critical Review

Assessing the Ecological Risks of Per- and Polyfluoroalkyl Substances: Current State-of-the Science and a Proposed Path Forward

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Abstract: Per- and poly-fluoroalkyl substances (PFAS) encompass a large, heterogenous group of chemicals of potential concern to human health and the environment. Based on information for a few relatively well-understood PFAS such as perfluorooctane sulfonate and perfluorooctanoate, there is ample basis to suspect that at least a subset can be considered persistent, bioaccumulative, and/or toxic. However, data suitable for determining risks in either prospective or retrospective assessments are lacking for the majority of PFAS. In August 2019, the Society of Environmental Toxicology and Chemistry sponsored a workshop that focused on the state-of-the-science supporting risk assessment of PFAS. The present review summarizes discussions concerning the ecotoxicology and ecological risks of PFAS. First, we summarize currently available information relevant to problem formulation/prioritization, exposure, and hazard/effects of PFAS in the context of regulatory and ecological risk assessment activities from around the world. We then describe critical gaps and uncertainties relative to ecological risk assessments for PFAS and propose approaches to address these needs. Recommendations include the development of more comprehensive monitoring programs to support exposure assessment, an emphasis on research to support the formulation of predictive models for bioaccumulation, and the development of in silico, in vitro, and in vivo methods to efficiently assess biological effects for potentially sensitive species/endpoints. Addressing needs associated with assessing the ecological risk of PFAS will require cross-disciplinary approaches that employ both conventional and new methods in an integrated, resource-effective manner. *Environ Toxicol Chem* 2020;00:1–42. © 2020 The Authors. *Environmental Toxicology and Chemistry* published by Wiley Periodicals LLC on behalf of SETAC. This article has been contributed to by US Government employees and their work is in the public domain in the USA.

Keywords: Per- and poly-fluoroalkyl substances; Ecological risk; Review; Strategy

BACKGROUND AND INTRODUCTION

Per- and poly-fluoroalkyl substances (PFAS) have achieved prominence in terms of public visibility and regulatory concern not seen since endocrine-disrupting chemicals were identified as a potential widespread risk to human health and the environment more than 2 decades ago (Hotchkiss et al. 2008).

This article includes online-only Supplemental Data.

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Select PFAS ERA Activities Around the World

- Canada
  - National ERAs for PFOS, PFOA, >C9 PFCAs
  - FEQG for PFOS
- Australia/New Zealand
  - Freshwater effects guidelines for PFOS, PFOA
- European Union
  - Multiple PFOS guideline values for freshwater effects
- United States
  - Development of ALC (EPA)/Screening Values (DoD) for PFOS, PFOA
  - State guidelines for aquatic/wildlife effects (MI, MN)

Exposure Assessment: What’s known and needed?

- PFAS present in variety of environmental matrices and biota
- Sometimes associated with point sources/applications, but also found in remote environments (e.g., Arctic)
- Large database for PFOS and PFOA, less (no) information for other PFAS
- Systematic monitoring data needed
  - Probabilistic sampling in variety of ecosystems
  - Data for larger diversity of PFAS
- Important role for nontargeted analytical techniques

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Exposure Assessment: The Bioaccumulation Challenge

- Key concern/need for both ecological and human health assessments
- Some PFAS classified as POPs based on bioaccumulation; evidence of biomagnification at higher trophic levels
- Processes controlling PFAS bioaccumulation uncertain
- Lipid-based models used to predict accumulation of nonionic organics (e.g., PCBs) not appropriate for PFAS
- Data concerning protein binding, metabolism, etc. needed to build mechanistic models based on structure
- Empirical relationships (BAFs, TTFs) may be best current option to predict bioaccumulation, but data limited to a few PFAS

What do we know about *in vivo* eco-relevant effects?

ECOTOX Knowledgebase

- Existing data helps define
  - Sensitive and susceptible species
  - Benchmarks and thresholds for ecological effects
- ECOTOX maintained by Duluth lab for >30 years (50,000+ papers)
- ECOTOX literature search and systematic review process completed for **>400 PFAS** (April 2018 - present)
- Ecological toxicity data from **1000 references**:
  - **159 PFAS**
  - **600 species**

	PFAS data in ECOTOX		
Group	# of Compounds	# of References	# of Records
All Species	159	1,118	29,797
Fish	115	320	10,560
Insects/Spiders	31	387	5,898
Flowers, Trees, Shrubs, Ferns	53	118	3,792
Birds	41	55	1,940
Crustaceans	43	78	1,900
Worms	32	64	1,857
Algae	46	60	997
Amphibians	24	35	879
Molluscs	23	29	643
Other Invertebrates	26	26	576
Mammals	19	18	389
Fungi	5	31	266
Reptiles	2	3	86
Miscellaneous	3	2	14

Updated from EPA on April 29, 2022

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In vivo Effects: Data Gaps and Limitations

- Limited/no data for majority of PFAS; no information for some classes
- Much of testing done (e.g., PFOS, PFOA) focused on acute lethality not sublethal chronic effects (growth, reproduction)
- Limited data in amphibians, birds, reptiles, mammalian wildlife
- Little to no toxicity data for most invertebrate taxa, plants
- Experimental issues with many aquatic studies done to date
  - PFAS in controls, unnecessary use of solvents, static-renewal (vs flow-through)
  - Analytical verification of PFAS concentration/dose often lacking
- <u>Field studies documenting effects (or not) sparse</u>

Defining a Path Forward: *In vivo* Testing

- Testing gaps abound (chemical, taxa, endpoints, lab/field) but not reasonable to address them solely through empirical testing
- Requires strategic prioritization supported by predictive tools to focus testing
  - Production volume/use, persistence, metabolism
  - Predicted/measured toxicity, bioactivity
- Identify of a "core" group of PFAS representative of different classes, and suite of potentially susceptible taxa/endpoints for "baseline" testing
  - Confirm/characterize exposure in test media and tissues

New Approach Methodologies (NAMs) for PFAS ERA

- Provides basis for predictive assessment of chemicals with limited information
  - Curated databases with existing knowledge ("read-across")
  - In silico (e.g., QSAR) models
  - Tools for cross-species extrapolation of effects
  - In vitro (including high throughput; HTP) measures of bioactivity
  - Pathway-based measurements from short-term in vivo assays (incl. 'omics)

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Employing NAMs for Assessing PFAS Risks

- Currently feasible applications
  - Prioritization (e.g., predicting/measuring bioactivity)
  - Categorization/fingerprinting
  - Guiding testing (e.g., species/endpoint selection)
- Not yet viewed as suitable for quantitative hazard/risk assessment
- Technical uncertainties
  - Tools/assays have limited taxonomic scope (e.g., mammalian-based HTP)
- Regulatory acceptance
  - Linkage to adverse apical effects uncertain

Adverse Outcome Pathways (AOPs) in PFAS ERAs

- Depict causal response linkages across biological levels of organization
- Developed specifically to support use of data from NAMs for effects prediction
- Provides framework to assemble and share knowledge (AOP Wiki)
- Multiple ongoing efforts supporting eco-AOP development for PFAS
  - Fish, amphibians, birds, invertebrates

Assessing Ecological Risks of PFAS Mixtures

- PFAS both enter and occur in most environments as complex mixtures
- Little testing with either formulations or component (synthetic) mixtures
- Mixture testing needs
    - Defining specific PFAS "driving" toxicity of mixtures (concentration, potency)
    - MOA/AOP-based categorization to support predictive models
- Develop/deploy nontargeted analytical techniques to identify unknown PFAS (incl. degradates, metabolites)

Summary/Recommendations

- PFAS present plausible risks to ecological systems and services
- Understanding risk requires both prospective and retrospective analysis
- Existing approaches for exposure/effects assessments conceptually valid but require “tailoring” to properties of PFAS
  - Toxicity assessments (in vitro/in vivo, endpoints, taxa)
  - Bioaccumulation (assays, empirical/mechanistic models)
- Data to conduct complete ERAs lacking for majority of PFAS
- Integrated predictive and empirical approaches needed to prioritize PFAS and guide PFAS testing

Publications from the workshop

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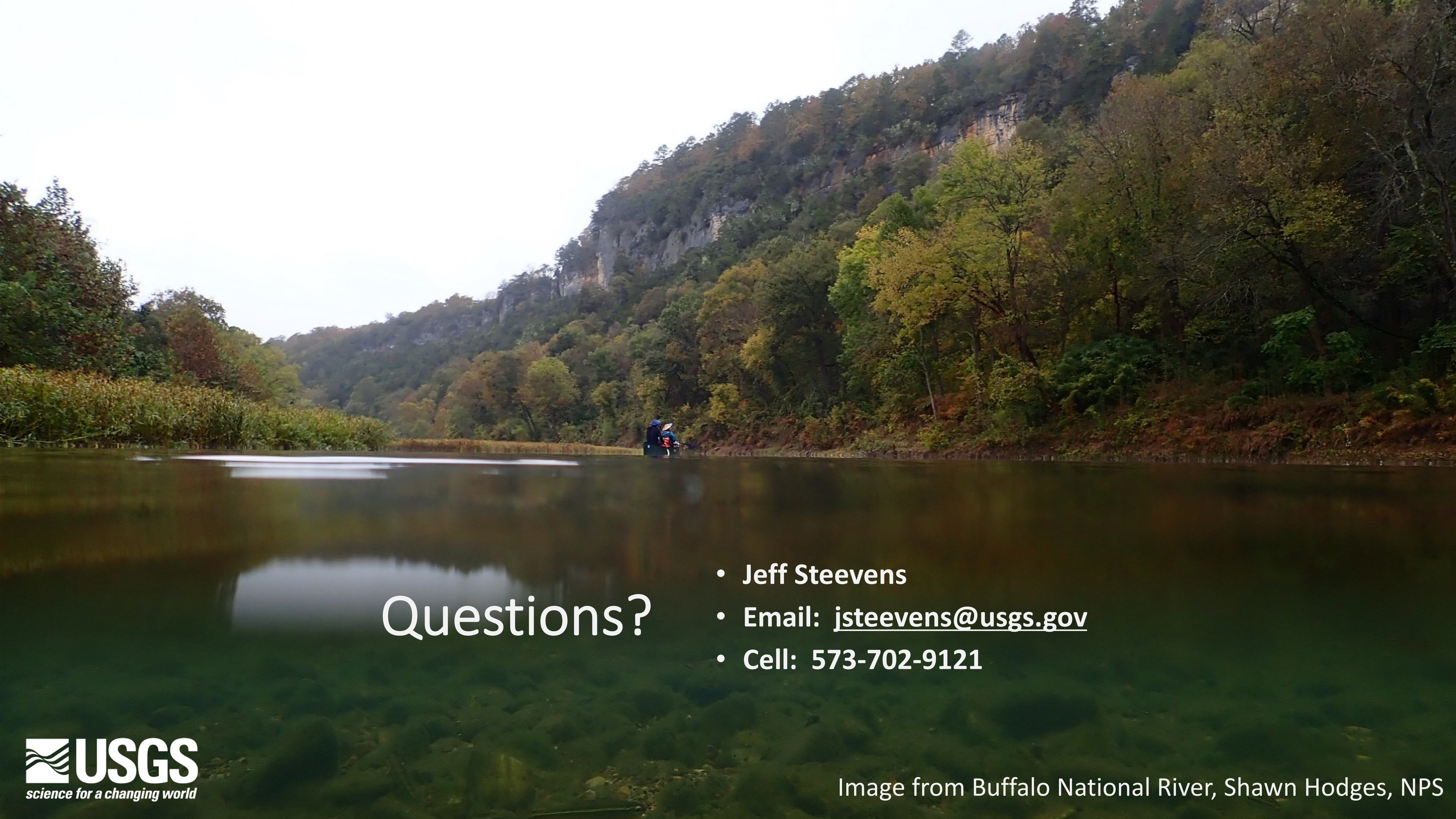

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Image from Buffalo National River, Shawn Hodges, NPS