Centers for Disease Control

Agency for Toxic Substances and Disease Registry Extramural Research Program Office

Multi-Site Study of the Health Implications of Exposure to PFAS-Contaminated Drinking Water

RFA-TS-19-002

Application Due Date: 06/03/2019

Multi-Site Study of the Health Implications of Exposure to PFAS-Contaminated Drinking Water

RFA-TS-19-002

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Part 1. Overview Information

Participating Organization(s)

Centers for Disease Control

Components of Participating Organizations

Agency for Toxic Substances and Disease Registry Extramural Research Program Office (ATSDR ERPO)
Agency for Toxic Substances and Disease Registry (ATSDR)

Notice of Funding Opportunity (NOFO) Title

Multi-Site Study of the Health Implications of Exposure to PFAS-Contaminated Drinking Water

Activity Code

Applications in response to this Notice of Funding Opportunity (NOFO) will be funded using the U01 activity code.

Notice of Funding Opportunity Type

New

Agency Notice of Funding Opportunity Number

RFA-TS-19-002

Assistance Listings (CFDA) Number(s)

93.070

Category of Funding Activity:

Health

NOFO Purpose

The Agency for Toxic Substances and Disease Registry (ATSDR) is soliciting research to commence a multi-site study on the human health effects of exposures to drinking water contaminated with per- and polyfluoroalkyl substances (PFAS). Proposed study sites must include communities using PFAS-contaminated private residential wells or public water systems. Exposure assessment will be based on measured PFAS serum levels as well as estimated PFAS serum levels derived from pharmacokinetic modeling of reconstructed PFAS drinking water concentrations over time. Effect biomarkers such as lipids and tests of immune and thyroid function derived from pharmacokinetic modeling of reconstructed PFAS drinking water concentrations over time will be evaluated.

ATSDR intends this research to be a two-part program consisting of (1) a mandatory core research protocol to allow ATSDR to aggregate the core data and to compare laboratory and statistical analyses across sites, and (2) each successful awardee will have the option to propose additional investigator-initiated research questions and hypotheses related to the overall goals of this NOFO.

The purpose of Amendment 1 to this NOFO is to correct the review criteria and headings from Section V, to add an Area of Joint Responsibility in Section VI (4), and to provide additional clarifying information based on questions received from potential applicants during the Pre-Application Conference Call held on April 29, 2019. The corrected review criteria and headings, the additional Area of Joint Responsibility, and a summary of the questions and

answers from the Pre-Application Conference Call can be found in Section VIII. Other Information, of the amended NOFO.

Key Dates

Publication Date: **To receive notification of any changes to RFA-TS-19-002, return to the synopsis page of this announcement at www.grants.gov and click on the "Send Me Change Notification Emails" link. An email address is needed for this service.**

Letter of Intent Due Date: **05/03/2019**

A letter of intent is not required to apply to this NOFO, is not binding, and does not enter into the review of a subsequent application. However, the information that it contains allows ATSDR staff to estimate the potential review workload and plan the review.

Application Due Date: **06/03/2019**

On-time submission requires that electronic applications be error-free and made available to CDC for processing from the NIH eRA system on or before the deadline date. Applications must be submitted to and validated successfully by Grants.gov no later than 5:00 PM U.S. Eastern Time. Applications must be submitted using the Application Submission System & Interface for Submission Tracking (ASSIST) module which is a web-based service used for the preparation and submission of grant applications to CDC through Grants.gov. ASSIST provides the ability for applicants to prepare their applications online, and offers the applicant additional capabilities including the ability to preview the application image, validate the application against required business rules, and prepopulate data from an applicant organization's records, therefore identifying issues earlier in the application submission process.

Note: HHS/CDC grant submission procedures do not provide a grace period beyond the application due date time to correct any error or warning notices of noncompliance with application instructions that are identified by Grants.gov or eRA systems (i.e., error correction window).

Scientific Merit Review: **07/24/2019**

This is an estimated date.

Secondary Review: **09/06/2019**

This is an estimated date.

Estimated Start Date: **10/01/2019**

Expiration Date: **06/28/2019**

Due Dates for E.O. 12372: **Due no later than 60 days after the application receipt date.**

Required Application Instructions

ELECTRONIC APPLICATION SUBMISSION VIA ASSIST IS PREFERRED

It is recommended that applicants use ASSIST for the electronic preparation and submission of applications through Grants.gov to CDC. ASSIST is an alternative method to prepare and submit applications, and provides many features to facilitate the application submission process which improves data quality (e.g., pre-population of organization data, pre-submission validation of business rules, and preview of the application image used for review). Use of the Grants.gov downloadable Adobe application packages and submission process will still be supported.

It is critical that applicants follow the instructions in the SF 424 (R&R) Application Guide except where instructed to do otherwise in this NOFO. Conformance to all requirements (both in the Application Guide and the NOFO) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Note: The Research Strategy component of the Research Plan is limited to 20 pages.

Applications that do not comply with these instructions may be delayed or not accepted for review.

Telecommunications for the Hearing Impaired: TTY 1-888-232-6348

Executive Summary

The Agency for Toxic Substances and Disease Registry (ATSDR) is committed to protecting people's health from environmental hazards by investigating the relationship between environmental factors and health, developing guidance, and building partnerships to support healthy decision making. The intent of the ATSDR extramural research program is to fund research that promotes healthy community environments by assessing the available scientific data to determine whether or not people are at risk because of their exposures to harmful chemicals in the environment.

Purpose: The Agency for Toxic Substances and Disease Registry (ATSDR) is soliciting research to commence a multi-site study on the human health effects of exposures to drinking water contaminated with per- and polyfluoroalkyl substances (PFAS). Proposed study sites must include communities using PFAS-contaminated private residential wells or public water systems. Exposure assessment will be based on measured PFAS serum levels as well as estimated PFAS serum levels derived from pharmacokinetic modeling of reconstructed PFAS drinking water concentrations over time. Specifically, grant awardees will be required to conduct historical reconstruction/water modeling in order to determine the PFAS concentration.

Effect biomarkers such as lipids and tests of immune and thyroid function derived from pharmacokinetic modeling of reconstructed PFAS drinking water concentrations over time will be evaluated.

ATSDR intends this research to be a two-part program consisting of (1) a mandatory core research protocol to allow ATSDR to aggregate the core data and to compare laboratory and statistical analyses across sites, and (2) each successful awardee will have the option to propose additional investigator-initiated research questions and hypotheses related to the overall goals of

this NOFO.

Successful awardees will be expected to send all serum and urine samples to an ATSDR facility or an ATSDR-designated facility for analysis. ATSDR will provide recipients with details regarding sample transfer within the first six months post award. All data resulting from the sample analysis will be stored by ATSDR. ATSDR will share each site's sample testing results with them in addition to additional de-identified data for all sites.

Research Notice of Funding Opportunity (NOFO) RFA-TS-19-002 aligns with the National Center for Environmental Health (NCEH)/ATSDR 2014-2016 strategic plan, available at https://www.atsdr.cdc.gov/about/mission_vision_goals.html, and supports the specific ATSDR goal to identify, characterize, and monitor health outcomes and environmental exposures to guide actions that protect and promote health. Research under this NOFO also aligns with the specific ATSDR goal to ensure safe drinking water. Additional information about ATSDR priorities is available at https://www.atsdr.cdc.gov/about/docs/NCEHATSDR_priorities_2014_final.pdf.

Mechanism of Support

The funding mechanism for this Notice of Funding Opportunity (NOFO) will be a cooperative agreement research grant.

Funds Available and Anticipated Number of Awards.

ATSDR intends to commit approximately $6,500,000 in FY 2019 to fund up to six applications. Awards issued under this NOFO are contingent upon availability of funds and a sufficient number of meritorious applications. Because the nature and scope of the proposed research will vary from application to application, it is also anticipated that the size and duration of each award may also vary. The total amount awarded and the number of awards will depend upon the number, quality, duration and cost of the applications received and approved.

Budget and Project Period.

The maximum award amount will be $3,000,000 per award for the first 12 month budget period. This includes both direct and indirect costs. An applicant may request a project period of up to five years. The maximum total project funding amount is $32,500,000 (including both direct and indirect costs) over the expected project period length, with a maximum of $3,000,000 per award per year. The project period for this award is expected to run from 10/01/2019 to 9/30/2024.

Throughout the project period, ATSDR's commitment to continuation of awards will be conditional on the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports), and the determination that continued funding is in the best interest of the Federal government.

Application Research Strategy Length: Page limits for the Research Strategy are clearly specified in Section IV. Application and Submission Information of this announcement.

Eligible Institutions/Organizations. Institutions/organizations listed in Section III. 1 are eligible to apply.

Eligible Project Directors/Principal Investigators (PDs/PIs). Individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution/organization to develop an application for support. NOTE: CDC/ATSDR does

not make awards to individuals directly.

Number of PDs/PIs. An application may name more than one PD/PI; their names must appear on the face page of the application. However:

- One (1) principal investigator must be designated as the contact PI for all correspondence related to the application.
- All PD/PIs must include their eRA Commons Identification in the Credential Field of the Senior/Key Person Profile Component of the SF424 (R&R) Application Package.
- Institutions/organizations proposing multiple PDs/PIs must visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF 424 (R&R) Application Guide.

Number of Applications. Applicant organizations may submit more than one application, provided that each application is scientifically distinct. However, applicant institutions can submit only one grant application with the same principal investigator in response to this NOFO. Only one application per principal investigator will be funded under this NOFO. Additionally, applicant institutions submitting applications with essentially the same proposed research to two or more CDC NOFOs will not be funded under more than one NOFO**.**

Application Type. NEW

Special Date(s). A pre-application teleconference call will be conducted on April 29, 2019 to address questions from prospective applicants regarding NOFO RFA-TS-19-002, "Multi-Site Study of the Health Implications of Exposure to PFAS-Contaminated Drinking Water". The call will begin at 1:00 PM Eastern Standard Time (EST) and end at 2:00 PM Eastern Standard Time (EST), or sooner if all questions are addressed. Questions and answers from the discussion will be included in an amended NOFO approximately 2 weeks after the call.

Participant Access Information

- Call Date: April 29, 2019
- Call Start Time: 1:00 PM Eastern Standard Time (EST)
- Call End Time: 2:00 PM Eastern Standard Time (EST)
- Call Leader: Daniel Holcomb, Scientific Program Official
- Toll-Free Number: 1-866-916-0413
- Conference Passcode: 52108552

Application Materials. See Section IV.1 for application materials.

Hearing Impaired. Telecommunications for the hearing impaired are available at: TTY: (770) 488-2783.

Part 2. Full Text

Section I. Funding Opportunity Description

Statutory Authority

This program is authorized by Section 316 of the National Defense Authorization Act for Fiscal

Year 2018 (Pub.L. 115-91) as amended by Section 315 of the John S. McCain National Defense Authorization Act for Fiscal Year 2019 (Pub. L. 115-232).

ATSDR is authorized to conduct the PFAS multi-site study under Section 316(a) of the 2018 National Defense Authorization Act (Public Law 115-91) for research in general, under the 1980 Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), as amended by the 1986 Superfund Amendments and Reauthorization Act (SARA) (42 U.S.C. 9601, 9604).

1. Background and Purpose

Background

Per-and polyfluorinated substances (PFAS) are a family of more than 4,500 chemicals. They are used in a variety of industrial and consumer applications and products, including: fire-fighting foams; personal care and cleaning products; as well as oil, stain, grease, and water-repellent coatings on carpet, textiles, leather, and paper. Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) are the most extensively studied. There is little toxicity data related to other PFAS chemicals. Although the scientific evidence linking PFAS exposures with adverse health effects is rapidly growing, it is inconsistent for a variety of reasons, including differences in exposure levels, PFAS evaluated, PFAS mixtures, and the outcomes measured.

Finding a measurable amount of PFAS in serum does not imply that the levels of PFAS cause an adverse health effect. Biomonitoring studies on levels of PFAS provide physicians and public health officials with reference values so that they can determine whether people have been exposed to higher levels of PFAS than are found in the general population. Biomonitoring data can also help scientists plan and conduct research on exposure and health effects.

Due to past environmental contamination, PFAS have been detected in numerous public and private drinking water systems throughout the United States. As a result, public health agencies and community organizations are concerned about the possible health risks for communities exposed to these drinking water supplies as well as other sources of PFAS contamination (e.g. dust, fish, food wrappers, etc.). In 2016, the EPA established a lifetime health advisory level (i.e. “the level below which adverse health effects are not anticipated to occur over a lifetime of exposure”) of 70 parts per trillion (ppt) in drinking water for PFOA and PFOS, either separately or combined.

Epidemiological studies have been conducted to assess the relationship between PFAS exposure and adverse health effects in humans. These studies have been conducted in occupationally exposed populations, residential populations exposed to PFAS through contaminated drinking water, and the general US population. These studies have generated concerns among communities with identified exposures to PFAS. Although the scientific evidence linking PFAS exposures with adverse health effects is rapidly growing, only a limited number of studies currently exist for some health endpoints. Inconsistencies may also occur for some health endpoints such as kidney biomarkers and reproductive outcomes due to biases resulting from the use of cross-sectional PFAS serum measurements to determine exposure. Such biases can be minimized if PFAS serum levels are estimated (e.g., based on historical reconstruction modeling of drinking water PFAS contamination and pharmacokinetic modeling).

The C8 (PFOA) studies conducted in West Virginia and Ohio communities surrounding a chemical plant that contaminated drinking water included a large cohort of highly exposed workers and residents (60,000+) and provided extensive and high-quality information. However, the studies focused primarily on PFOA, and to a lesser extent, PFOS. Except for the C8 studies, there is scant information on the health effects of exposures to PFAS-contaminated drinking water. This research gap has led to the need for more epidemiological research on the health effects of PFAS exposures.

Purpose

The Agency for Toxic Substances and Disease Registry (ATSDR) is soliciting research to commence a multi-site study on the human health effects of exposures to drinking water contaminated with per- and polyfluoroalkyl substances (PFAS). Proposed study sites must include communities using PFAS-contaminated private residential wells or public water systems. Exposure assessment will be based on measured PFAS serum levels as well as estimated PFAS serum levels derived from pharmacokinetic modeling of reconstructed PFAS drinking water concentrations over time. Specifically, grant awardees will be required to conduct historical reconstruction/water modeling in order to determine the PFAS concentration.

Effect biomarkers such as lipids and tests of immune and thyroid function derived from pharmacokinetic modeling of reconstructed PFAS drinking water concentrations over time will be evaluated.

ATSDR intends this research to be a two-part program consisting of (1) a mandatory core research protocol to allow ATSDR to aggregate the core data and to compare laboratory and statistical analyses across sites, and (2) each successful awardee will have the option to propose additional investigator-initiated research questions and hypotheses related to the overall goals of this NOFO.

Successful awardees will be expected to send all serum and urine samples to an ATSDR facility or an ATSDR-designated facility for analysis. ATSDR will provide recipients with details regarding sample transfer within the first 6 months post award. All data resulting from the sample analysis will be stored by ATSDR. ATSDR will share each site's sample testing results with them in addition to additional de-identified data for all sites.

References:

ATSDR. Feasibility Assessment for Epidemiological Studies at Pease International Tradeport, Portsmouth, New Hampshire, November, 2017. Available at: https://www.atsdr.cdc.gov/sites/pease/documents/Pease_Feasibility_Assessment_November-2017_508.pdf

ATSDR. Per- and Polyfluoroalkyl Substances (PFAS) and Your Health, November, 2018. Available at: https://www.atsdr.cdc.gov/pfas/index.html

ATSDR. Toxicological Profile for Perfluoroalkyls, August, 2018. Available at: https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=1117&;tid=237

Centers for Disease Control and Prevention, National Biomonitoring Program. Per- and Polyfluorinated Substances (PFAS) Factsheet, April, 2017. Available at: https://www.cdc.gov/biomonitoring/PFAS_FactSheet.html

Sunderland EM, Hu XC, Dassuncao C, Tokranov AK, Wagner CC, Allen JG. A Review of the Pathways of Human Exposure to Poly- and Perfluoroalkyl Substances (PFASs) and Present Understanding of Health Effects; J Expo Sci Environ Epidemiol; 2018; Nov 23, (Epub ahead of print)

Healthy People 2020 and other National Strategic Priorities

ATSDR is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2020" and to measuring program performance as stipulated by the Government Performance and Review Act (GPRA). This research NOFO directly supports the United States Department of Health and Human Services (DHHS) Healthy People 2020 goals and objectives as described in: http://www.healthypeople.gov/.

The proposed program of research addresses the Healthy People 2020 priority area of environmental health infrastructure and surveillance and is in alignment with ATSDR's performance goal to conduct a targeted program of research to identify, characterize, and monitor health outcomes and environmental exposures to guide actions that protect and promote health. Specifically this research NOFO supports the Healthy People 2020 goal for promoting high-quality, longer lives free of preventable disease and Healthy People Objective EH-21 to improve the quality, utility, awareness, and use of existing information systems for environmental health.

Public Health Impact

The results of this study will add to the body of literature regarding the association between PFAS exposure in drinking water and health outcomes. Since the study will evaluate PFAS serum levels and adverse health outcomes, the study findings are expected to be generalizable among individuals with similar PFAS serum levels who have been exposed to PFAS contaminated drinking water, as well as those potentially exposed from other sources (e.g., diet, workplace exposures).

Relevant Work

NCEH/ATSDR provides ongoing technical assistance to affected state/city/local health departments in conducting PFAS exposure investigations on an as-needed basis. NCEH/ATSDR has initiated a proof of concept research study to inform the approach outlined here. That proof of concept will be conducted at Pease International Tradeport in Portsmouth, NH. NCEH/ATSDR also plans to conduct PFAS exposure assessments in no less than eight sites with PFAS contaminated drinking water which are yet to be determined.

ATSDR also has extensive experience in modeling the fate and transport of contaminants in groundwater from the source of the contamination to drinking water supply wells and distribution system (i.e. from previous work performed under the USMC Camp Lejeune project and the Toms River study). ATSDR has reconstructed historical concentrations of trichloroethylene, tetrachloroethylene and other volatile organic chemicals in the drinking water systems at Camp LeJeune, North Carolina and in Decatur, Alabama. ATSDR has experience using a pharmacokinetic model to estimate chemical half-lives of per fluoro octanoic acid (PFOA), perfluorooctane sulfonate (PFOS) and perfluorohexane sulfonic acid and its salts (PFHxS) in serum. ATSDR will use this modeling expertise to advise and assist recipients in reconstructing historical PFAS concentrations in drinking water and serum levels.

References:

Maslia, ML; Aral MM; Ruckart, PZ; Bove, FJ. Reconstructing Historical VOC Concentrations in Drinking Water for Epidemiological Studies at a U.S. Military Base: Summary of Results. Water (Basel) 2016; 8(10):449.

Maslia, ML; Reyes, JJ; Gillig, RE; Sautner, JB; Fagliano, JA; Aral, MM; Public Health Partnerships Addressing Childhood Cancer Investigations: Case Study of Toms River, Dover Township, New Jersey, USA. Int J Hyg Environ Health; 2005; 208(1-2):45-54.

Worley, RR; Yang, X; Fisher, J; Physiologically Based Pharmacokinetic Modeling of Human Exposure to Perfluorooctanoic Acid Suggests Historical Non-drinking-water Exposures are Important for Predicting Current Serum Concentrations. Toxicol Appl Pharmacol; 2017; 330:9-21.

2. Approach

This is cooperative research program will include several research components (core, optional, and future). First, all recipients must conduct research at their sites following the ATSDR core protocol. This core protocol has been submitted for final approval, but a link to the current version is provided in this document for applicants' planning purposes. Uniform collections under the core protocol will allow ATSDR and recipients to aggregate data and analyze results across sites.

At each selected site, the core research activities will focus on assessing health outcomes among adults and children exposed to PFAS-contaminated drinking water. As part of the core activities, the successful applicants will obtain blood samples from participants to measure PFAS serum levels and effect biomarkers. Applicants will be expected to describe how they intend to characterize the participants' exposures based on the measured serum concentrations of PFAS compounds and on modeled estimated current and historical PFAS serum levels (e.g., referent or low, medium, high). Successful awardees will be required to conduct historical reconstruction(s) of PFAS concentrations in drinking water and pharmacokinetic modeling. Specifically, grant awardees will be required to conduct historical reconstruction/water modeling in order to determine the PFAS concentration.

As part of the core activities, applicants should also plan to obtain urine samples from participants to measure urinary PFAS levels and kidney function, as they are identified during the program period, and to archive these blood and urine samples in order to provide for the possibility to conduct subsequent analyses of additional PFAS chemicals and effect biomarkers. Successful grantees will be expected to send all serum and urine samples to an ATSDR facility or an ATSDR-designated facility. ATSDR will provide recipients with details regarding sample transfer within the first 6 months post award. All data resulting from the sample analysis will be stored by ATSDR. ATSDR will share each site's sample testing results with them in addition to additional de-identified data for all sites.

Applicants may propose their own site-specific modules to investigate their own research interests related to the required core activities.

Applicants should plan to obtain consent from participants to archive leftover blood and urine samples in order to provide for the possibility to conduct analyses of additional PFAS chemicals

and effect biomarkers. Successful grantees will be expected to send all serum and urine samples to an ATSDR facility or an ATSDR-designated facility. ATSDR will provide recipients with details regarding sample transfer within the first six months post award. All data resulting from the sample analysis will be stored by ATSDR. ATSDR will share each site's sample testing results with them in addition to additional de-identified data for all sites.

Applicants should describe a community engagement plan in their application and consider requesting assistance from local and state health departments in their proposed recruitment efforts, and plan to engage community organizations to assist in conducting outreach about the study and recruitment of participants. In addition, the applicant should consider engaging with the affected community in decisions related to outreach about the study, participant recruitment strategies, study logistics, and dissemination of study findings.

Approach Considerations for Achieving Primary Outcomes

Applicants will be required to describe how they plan to conduct historical reconstruction/water modeling in order to determine the PFAS concentration in the drinking water and the exposure estimation. In order to determine the level of complexity of modeling necessary to historically reconstruct PFAS drinking water contamination, the successful applicants should collect all the available historical and current information on the water system (e.g., distribution system characteristics and sources of water, supply well construction and production logs, well capacity, and years of operation, water demand and pipe network, etc.) and/or private wells. The successful applicants should also collect all available information on the source and migration of the PFAS contamination (e.g., information on the historical use of AFFF or PFAS in industrial processes, information on PFAS emissions to soil, ground water and surface water, hydrogeological reports, and information on groundwater plumes, etc.) and PFAS sample data from supply wells, private wells, monitoring wells, surface water, and the distribution system.

Child and adult studies proposed should be cross-sectional with separate evaluation of children (ages 4-17 years) and adults (aged ≥18 years). The participants should be recruited from areas served by PFAS-contaminated drinking water. The study goal is to recruit, at least 2,000 children and 6,000 adults at a minimum in total.

Required sampling frame – Please refer to the draft ATSDR core study protocol document located https://www.atsdr.cdc.gov/PFAS/PFAS-Research-NOFO.html

For sites with a contaminated public water supply, the successful applicants should request, at a minimum:

- information from the water purveyor on the distribution system characteristics, in particular, whether the PFAS concentrations can be assumed to be relatively uniform throughout the system or whether the system had specific areas with considerably higher or lower PFAS concentrations, and
- a list of residences served by the water purveyor, including the name of the person on the residential account and the street address of the residence.

If uniform PFAS concentrations can be assumed, then a random sample of households may be conducted. Recruitment methods could include recruitment letters mailed to potentially affected

households. If the system has areas with considerably higher PFAS concentrations, then the successful applicants could target (oversample) households in these areas for recruitment letters.

For sites with contaminated private wells, applicants should request information on the impacted residences and the results of PFAS sampling of their private wells from the state and/or local health and environmental agencies. Sampling should target households based on the magnitude of the PFAS concentrations in their private wells – i.e., wells with higher concentrations should be oversampled.

Partnerships between the applicant institution and outside entities may be necessary to complete the proposed work. However, a substantial portion of the proposed research work plan must be carried out by the applicant organization throughout the project period and the applicant organization cannot serve as a "pass through" to fund another entity to conduct the majority of the research. If partnerships are necessary, applicants are required to provide documentation that clearly describes how the partnership will allow the applicants to complete the proposed work (e.g., letter of support from institution or agency pledging access to data for outcome measures; Memorandum of Understanding outlining partner commitment of or access to resources relevant to the application's research plan). Documentation describing working partnerships must clearly describe the existing working relationship, plans for the proposed research, the nature and extent of the involvement to be provided by the applicant institution and outside entity, including the roles and responsibilities of the Principal Investigator(s) and the outside entities or partner agencies, the outside entity's scope of work, and how the partnership will ensure implementation and sustainability of the proposed research plan.

Data Collection Methods

The ATSDR core activities for data collection, at a minimum, are as follows:

- Obtain adult consent, and parental permission and child assent (ages 7 years and older), to participate in this research study.
- Obtaining and ensuring appropriate retention of identifiable study participant contact information for future research.
- Administer adult and child questionnaires, and seek medical records verification of self-reported diseases. The adult participants and the parents of the child participant will be asked to bring documentation of all current prescription and over the counter medications.
- Administer neurobehavioral test batteries to the children and their parent(s) and seek to abstract children’s school records (in particular, special education records).
- Obtain a blood sample from each participant for analyses of PFAS and a number of effect biomarkers.
- Seek consent to store residual blood samples for future analyses of other PFAS and/or relevant effect biomarkers yet to be identified.
- Collect a urine sample from all participants to be stored for future analyses for PFAS and/or relevant effect biomarkers.
- Determine whether study participants would be interested in being contacted for any future related studies.
- Enrollment of study participants, including determining eligibility, verifying study participants current contact information for results reporting, and potential future contact,

and obtaining informed consent.

Trained study staff will be required to perform the following measurements based on specific methods laid out in the ATSDR core sample study protocol, current draft available at https://www.atsdr.cdc.gov/PFAS/PFAS-Research-NOFO.html

- Body measurements (i.e. height, weight, and waist and hip circumference)
- Blood pressure measurements
- Blood draws
- Fasting blood specimen
- First morning urine void

Successful awardees will be required to coordinate with ATSDR staff on how and where to transfer samples for analysis. ATSDR will coordinate and house the data resulting from sample analysis (of the core) for all sites, and will provide individual site-specific data back to each site in addition to de-identified data collected from all sites.

Additionally, each adult participant and the parent of the child participant will be asked to verify and update their current contact information for results reporting and potential future contact.

ATSDR will provide a REDCap secure web application for building and managing online surveys and databases (at no cost to the awardee) that includes all ATSDR data requirements such as variable names, data types (numerical, text, drop-down list, etc.), controlled vocabulary, value range, and so on. The REDCap application provided by ATSDR will also contain a database for data storage, data entry forms for various study surveys/questionnaires, and data validation rules. ATSDR strongly encourages the awardees to use the REDCap application provided by ATSDR for data management. This will help ensure that data sets from different study sites share a standard data structure (variable name, type, coding, etc.) and can be integrated into the ATSDR central database automatically. If the awardees choose not to use the provided REDCap application due to technical or other reasons, awardees will be responsible for making sure their delivered data sets to be in the same data structure adopted by the ATSDR REDCap application. For more information on REDCap, please see https://www.project-redcap.org/.

Given the extent of ATSDR staff involvement in this research activity, it is anticipated that Office of Management and Budget (OMB) approval will be necessary before data collection can begin.

CDC/ATSDR may initiate a funding supplement to support additional activities in support of this research study. Pending availability of additional funds during the period of performance, successful applicants may have the opportunity to request supplemental funding for additional effort and/or innovative research intended to advance the science within scope of the approved research project, or a proposed change in scope. Such innovative research projects that may be funded with a supplement should be within scope of this NOFO, and may include research on PFAS exposure in relation to: sexual and neurodevelopment; bone density and osteoporosis measurements (such as ultrasound) in adults and children; liver disease imaging or biopsy in subjects with elevated liver enzymes other liver disease biomarkers (e.g. in addition to cytokeratin 18 (CK-18)); and reproductive health/fertility assessments. Any such supplements would be subject to review and approval by CDC/ATSDR staff.

Common Rule Requirements

On September 8, 2015, the Department of Health and Human Services (HHS) and 15 other federal departments and agencies published a notice of proposed rulemaking (NPRM) proposing revisions to each agency's codification of the Federal Policy for the Protection of Human Subjects, originally promulgated as a Common Rule in 1991. On January 19, 2017, HHS and other federal departments and agencies published a final rule revising the Federal Policy for the Protection of Human Subjects. (82 FR 7149). https://www.federalregister.gov/documents/2017/01/19/2017-01058/federal-policy-for-the-protection-of-human-subjects

The 2018 Common Rule Update has new requirements for cooperative research at Title 45 Code of US Federal Regulations, Part 46, and creates a requirement for U.S.-based institutions engaged in cooperative research to use a single Institutional Review Board (IRB) for that portion of the research that takes place within the United States, with certain exceptions. https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&;SID=83cd09e1c0f5c6937cd9d7513160fc3f&;pitd=20180719&;n=pt45.1.46&;r=PART&;ty=HTML

Successful awardees under this cooperative agreement will be subject to the new rules, including the need to collaborate in selecting a single IRB to review and approve all non-exempt human subjects research activities conducted under this cooperative agreement.

Objectives/Outcomes

Primary Outcomes to be achieved with this research:

This cooperative agreement will provide funding to successful awardees to to conduct data analysis and historical reconstruction, including water modeling, physiologically based pharmacokinetic (PBPK) modeling, and statistical analysis of the relationship between chemical exposure and health outcomes. Specifically, applicants should propose research designed to examine associations between exposures to PFAS compounds and lipids, and adverse health effects and/or outcomes on renal function and kidney disease, thyroid hormones and disease, liver function and disease, glycemic parameters and diabetes, as well as immune response and function in both children and adults. All applicants should propose to investigate, at a minimum, the effect of PFAS exposures on differences in sex hormones and sexual maturation, vaccine response, and neurobehavioral outcomes in children. In adults, research on additional health outcomes of interest could include cardiovascular disease, osteoarthritis and osteoporosis, endometriosis, and autoimmune disease.

ATSDR will consolidate and integrate all data from successful grantees to support epidemiological and statistical analyses, including those above at a larger scale (i.e., across multiple sites). Consent forms must be written to achieve these goals. A publication review committee established by ATSDR will prioritize and coordinate dissemination of study findings in the scientific literature and to the communities. This committee will include representatives from the successful grantees.

Expected Timeline for Activities and Deliverables

Maximum Number of	Completion of Expected Successful Awardee Activities

Months After Award	
6	Obtain the single IRB approval and/or rely on CDC/ATSDR IRB approval.
12 -18	Protocol completed and reviewed by CDC/ATSDR, for core activities and beyond, if applicable.
24	Complete site-specific data and sample collection including questionnaires and neurobehavioral testing. Send all samples to ATSDR and/or ATSDR-designated laboratory facility for analysis.
24-36	Complete historical water reconstruction.
36	Provide site-specific data to CDC/ATSDR; data management center at ATSDR creates combined/aggregated dataset from multi-site site specific datasets. Commence statistical analyses by recipients and CDC/ATSDR (in collaboration) on site-specific and aggregated dataset. Publication committee formed.
42	Complete statistical analyses of data; preliminary report prepared for CDC/ATSDR (review, clearance). Provide reports on individual test results to study participants.
48-54	Draft final report/preparation in collaboration with CDC/ATSDR.

Number of Months After Award	Expected Deliverables from Successful Awardees to CDC/ATSDR
6	Provide evidence of institution's IRB approval or rely on CDC/ATSDR IRB approval.
12 -18	Submit completed protocol for core activities and beyond, if applicable. Obtain approval from CDC/ATSDR.
24	Submit dataset including participants contact information, questionnaire data, neurobehavioral testing data.
24-36	Analyses of site-specific PFAS exposure and clinical tests/biomarkers shared with recipients; combined dataset created. Provide evidence of historical water reconstruction. Send all samples to ATSDR and/or ATSDR-designated laboratory facility for analysis.
42	Preliminary report on site-specific results.

48-54	Final report on site-specific result.

Target Population

The suggested eligibility criteria for children is as follows:

- Ages 4-17 years at the start of the study,
- Resided in areas with documented past or present PFAS drinking water concentrations at the tap, OR were exposed in-utero or during breastfeeding when the mother consumed contaminated drinking water
- Last exposure occurred no more than 15 years prior to the start of the study
- Exclusion of children whose birth mothers were ever employed as a firefighter, ever participated in fire training exercises using Aqueous Film-Forming Foam Concentrates (AFFF), or were ever employed in industrial facilities that used PFAS chemicals in the manufacturing process

The suggested eligibility criteria for adults is as follows:

- Ages ≥18 years at the start of the study
- Resided in areas with documented past or present PFAS drinking water concentrations at the tap,
- Last exposure occurred no more than 15 years prior to the start of the study,
- Exclude persons ever employed as a firefighter, ever participated in fire training exercises using AFFF foam, or ever employed at industrial facilities that used PFAS chemicals in the manufacturing process.

Collaboration/Partnerships

ATSDR has taken several steps to ensure scientific credibility, consistency, and validity of the overall extensive sample testing and analyses of exposure and clinical/biomarker components required to fulfil core protocol requirements.

As part of their core activities, the successful awardees will be required to have exposure analytes (i.e. PFAS) in human samples analyzed by the NCEH Division of Laboratory Sciences laboratory. ATSDR will bear all costs related with these analyses.

To minimize extensive cost and efforts to coordinate the analyses of number of clinical tests and research biomarkers, or the need to implement an inter-laboratory quality control or comparison program to ensure comparability and external validity of performed analyses, ATSDR will engage and contract a commercial laboratory (to be determined/designated by ATSDR) to provide logistical support, handling/shipping and most importantly the analyses of all requested analytes. Successful applicants will not be responsible for the cost of biomarker testing/analysis; ATSDR will directly fund a designated laboratory to complete this task.

Successful awardees will be required to use the same ATSDR-designated analytical laboratory to conduct the specific core clinical tests and research biomarkers listed in the ATSDR core study protocol (current draft available at https://www.atsdr.cdc.gov/PFAS/PFAS-Research-NOFO.html) to ensure the comparability and quality control of the analysis of samples received from the various research sites. Successful awardees will be responsible for properly shipping all samples

submitted for analysis to the ATSDR-designated laboratory. This will also assure the best possible analysis cost rates and effective use of funding. The cost of these analyses will be paid for by ATSDR.

The core activities also require conduct of an extensive battery of neuro-behavioral tests. It is not feasible to engage an outside entity to conduct all the tests at number of different sites. The successful awardees will be expected to coordinate and ensure that they use the same neuro-behavioral tests for comparison purposes among sites, as specified in the ATSDR study protocol. Successful awardees must describe in their proposed research plan how they intend to engage and retain qualified personnel to administer such tests (current draft available at https://www.atsdr.cdc.gov/PFAS/PFAS-Research-NOFO.html).

Partnerships between the applicant institution and outside entities may be necessary to complete the proposed work. However, a substantial portion of the proposed research work plan must be carried out by the applicant organization throughout the project period and the applicant organization cannot serve as a “pass through" to fund another entity to conduct the majority of the research. Applicant organizations may include collaborators or consultants from foreign institutions. All applicable federal laws and policies apply. For applications that include collaborators or consultants from foreign institutions, the majority of the proposed research work plan (e.g. at least 80%) must be carried out domestically by the applicant organization throughout the project period.

If partnerships are necessary, applicants are required to provide documentation that clearly describes how the partnership will allow the applicants to complete the proposed work (e.g., letter of support from institution or agency pledging access to data for outcome measures; Memorandum of Understanding outlining partner commitment of or access to resources relevant to the application's research plan). Documentation describing working partnerships must clearly describe the existing working relationship, plans for the proposed research, the nature and extent of the involvement to be provided by the applicant institution and outside entity, including the roles and responsibilities of the Principal Investigator(s) and the outside entities or partner agencies, the outside entity's scope of work, and how the partnership will ensure implementation and sustainability of the proposed research plan.

Applicants must describe all data sources and processes used to assure data access. Evidence of access to the data from outside entities may be demonstrated by data sharing agreements, Memoranda of Understanding or Letters of Support, detailing the data availability.

Documentation of collaboration/partnerships and data access must be included in the Letters of Support section of the application. **Applications that do not include appropriate Letters of Support or Memoranda of Understanding between the applicant organization and every outside entity that will be participating in the research or providing data access will be considered non-responsive and will not be forwarded for peer review.**

Evaluation/Performance Measurement

Applicants should include analytic plans that describe the research design and hypotheses, data collection measures, and methods to evaluate whether the proposed research plan can effectively address the hypotheses. Outcomes to be evaluated should be clearly specified. Performance measures should include the number of participants (children/adults) recruited into the study and the participation rate, the number of participants who provided a blood and urine sample, and the

number of children and parents who completed the neurobehavioral tests.

Translation Plan

Applicants should provide evidence of the potential for widespread dissemination, implementation, and sustainability of the proposed strategy to ensure that the approach, if effective, is scalable without prohibitive costs or resources. Research findings should be disseminated through publications, including articles in peer reviewed journals and research briefs for diverse audiences, as well as presentations at professional conferences and other venues. An explanation for how the scientific findings could be translated into public health programs, policies or practice should be included in the application.

Successful awardees will be required to attend at least one reverse site visit in Atlanta with ATSDR program staff during the period of performance to review their progress and findings and to discuss opportunities for widespread dissemination of their research achievements and lessons learned. Travel costs for attending this meeting must be included the application's travel budget submitted in response to this NOFO.

Section II. Award Information

Funding Instrument Type: Cooperative Agreement

A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, scientific or program staff will assist, guide, coordinate, or participate in project activities.

Application Types Allowed:

New - An application that is submitted for funding for the first time. Includes multiple submission attempts within the same round.

Revision (formerly Competing Supplement) - Request for additional funds for a current award to expand the scope of work. Applicants should contact the awarding agency for advice on submitting any revision/supplement application.

Estimated Total Funding: $32,500,000

Anticipated Number of Awards: 6

ATSDR intends, pending the availability of funds, to commit approximately $6,500,000 in FY 2019 to fund up to six (6) applications. Because the nature and scope of the proposed research will vary from application to application, it is also anticipated that the size and duration of each award may also vary. The total amount awarded and the number of awards will depend upon the number, quality, duration and cost of the applications received and approved.

Awards issued under this NOFO are contingent on the availability of funds and submission of a sufficient number of meritorious applications.

Award Ceiling:	$3,000,000 Per Budget Period
Award Floor:	$500,000 Per Budget Period
Total Period of Performance Length:	5 year(s)

Throughout the Period of Performance, CDC's commitment to continuation of awards will depend on the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports), and CDC's determination that continued funding is in the best interest of the Federal government.

HHS/CDC grants policies as described in the HHS Grants Policy Statement (http://www.hhs.gov/ sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf) will apply to the applications submitted and awards made in response to this NOFO.

Section III. Eligibility Information

1. Eligible Applicants

Eligibility Category:	State governments County governments City or township governments Special district governments Independent school districts Public and State controlled institutions of higher education Native American tribal governments (Federally recognized) Public housing authorities/Indian housing authorities Native American tribal organizations (other than Federally recognized tribal governments) Nonprofits having a 501(c)(3) status with the IRS, other than institutions of higher education Nonprofits without 501(c)(3) status with the IRS, other than institutions of higher education Private institutions of higher education For profit organizations other than small businesses Small businesses Unrestricted (i.e., open to any type of entity above), subject to any clarification in text field entitled "Additional Information on Eligibility"
Additional Eligibility Category:	

The following types of Higher Education Institutions are always encouraged to apply for CDC support as Public or Private Institutions of Higher Education:

Hispanic-serving Institutions
Historically Black Colleges and Universities (HBCUs)
Tribally Controlled Colleges and Universities (TCCUs)
Alaska Native and Native Hawaiian Serving Institutions

Nonprofits Other Than Institutions of Higher Education:

Nonprofits (Other than Institutions of Higher Education)

Governments:

U.S. Territory or Possession

Other:

Native American tribal organizations (other than Federally recognized tribal governments)
Faith-based or Community-based Organizations
Regional Organizations
Bona Fide Agents: A Bona Fide Agent is an agency/organization identified by the state as eligible to submit an application under the state eligibility in lieu of a state application. If applying as a bona fide agent of a state or local government, a legal, binding agreement from the state or local government as documentation of the status is required. Attach with "Other Attachment Forms."
Federally Funded Research and Development Centers (FFRDCs): FFRDCs are operated, managed, and/or administered by a university or consortium of universities, other not-for-profit or nonprofit organization, or an industrial firm, as an autonomous organization or as an identifiable separate operating unit of a parent organization. A FFRDC meets some special long-term research or development need which cannot be met as effectively by an agency's existing in-house or contractor resources. FFRDC's enable agencies to use private sector resources to accomplish tasks that are integral to the mission and operation of the sponsoring agency. For more information on FFRDCs, go to https://dap.dau.mil/acquipedia/Pages/ArticleDetails.aspx?aid=5e3079b8-44f2-43df-a0e7-9f379e8c48ed

2. Foreign Organizations

Foreign Organizations are not eligible to apply.

Foreign components of U.S. Organizations are not eligible to apply.

For this announcement, applicants may include collaborators or consultants from foreign institutions. All applicable federal laws and policies apply.

3. Special Eligibility Requirements

Applicant organizations may include collaborators or consultants from foreign institutions. All applicable federal laws and policies apply. For applications that include collaborators or consultants from foreign institutions, the majority of the proposed research work plan (e.g. at least 80%) must be carried out domestically by the applicant organization throughout the project period. For all applications a substantial portion of the proposed research work plan must be carried out by the applicant organization throughout the project period and the applicant organization cannot serve as a "pass through" to fund another entity to conduct the majority of the research.

Organizational Capacity:

Applicants must demonstrate the following organizational capacity elements to ensure they can successfully complete this study:

- Proven experience conducting drinking water exposure studies and publications related to water contamination.
- Proven capacity to conduct cross-sectional or cohort studies; epidemiological studies; conduct research in area of persistent pollutants and health (with focus on chronic disease and with expertise in children health; experience with PFAS is desired but not required).
- Plan for and evidence of having a range of experts (including a Principal Investigator) with experiences that will enable the work of this research study in accordance with the proposed study protocol (demonstrate support with resumes, etc.).
- Demonstrated capacity to establish and maintain community engagement programs within the community including a plan that describes “community engagement” activities.
- Experience in establishing, or a plan for establishing a Community Advisory group (demonstrated by MOU/MOA/LOIs).
- Demonstrated access and collaboration with state health authorities (i.e. State Health department, State Cancer registry) to access and use state/local data in research and public health setting (MOU required).
- Capacity and infrastructure in place to collect, manage and analyze data as specified in their proposed research protocol; conduct participant follow up; linking data; abstracting medical records data and/or special education information.
- Serve as or partner with analytical laboratory facilities for clinical or research biomarkers analyses and/or track record of such collaboration with established research or commercial laboratories as required by the research protocol for proposed research

work outside of the core activities.

This organizational capacity should be documented in the applicant's research strategy, key personnel biosketches, letters of support and appendices as appropriate.

4. Justification for Less than Maximum Competition

N/A

5. Responsiveness

Applicants must provide evidence that the proposed study site has documented past or present PFAS drinking water concentrations at the tap. **Applications where this site information evidence is not included will be considered non-responsive and will not be forwarded for peer review.**

Applicants must describe how historical reconstruction of PFAS concentrations in the drinking water will be accomplished including data sources and methods that will be used. A description of the source(s) of PFAS contamination in the drinking water must be included in the application. If the source is an industrial facility, then the description should include historical information about PFAS use at the facility and PFAS emissions into the environment. If the source is AFFF use, then the description should include historical information about the period and location of AFFF use and amount used. **Applications that do not meet this requirement will be considered non-responsive and will not be forwarded for peer review.**

The biosketch of the PI must include documentation of expertise and experience conducting epidemiological investigations involving the collection of biological samples for the analyses of exposure biomarkers and/or effect biomarkers. This expertise must be documented with at least one first-authored, peer-reviewed publication of epidemiological research reporting results from analyses of biological samples, or documented with experience as the PI for a grant for epidemiological research that included collection of biological samples, preferable for analyses of biomarkers of environmental exposures and/or health effects. **Applications that do not meet this requirement will be considered non-responsive and will not be forwarded for peer review.**

There must be an overall match between the proposed research objectives as described in the applicant's abstract and the research objectives of this announcement as described in Section I under the heading *Objectives/Outcomes.* **Applications that do not provide an overall match between the proposed research objectives (as described in the applicant's abstract) and the research objectives of this announcement (as described in Section I under the heading *Objectives/Outcomes*) will be considered non-responsive and will not be forwarded for peer review.**

Applicants must describe all data sources and processes used to assure data access. Evidence of access to the data from outside entities may be demonstrated by data sharing agreements, memoranda of understanding, or Letters of Support detailing the data availability. Documentation of collaboration/partnerships and data access must be included in the Letters of Support section of the application. **Applications that do not include appropriate Letters of Support or memoranda of understanding between the applicant organization and every outside entity that will be participating in the research or providing data access will be**

considered non-responsive and will not be forwarded for peer review.

6. Required Registrations

Applicant organizations must complete the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. Applicants must have a valid Dun and Bradstreet Universal Numbering System (DUNS) number in order to begin each of the following registrations.

- (Foreign entities only): Special Instructions for acquiring a Commercial and Governmental Entity (NCAGE) Code: https:// eportal.nspa.nato. int/ AC135Public/ Docs/ US%20Instructions%2 0for%20NSPA%20NCAGE.pdf
- System for Award Management (SAM) – must maintain current registration in SAM (the replacement system for the Central Contractor Registration) to be renewed annually, https://www.sam.gov/portal/SAM/.
- Grants.gov
- eRA Commons

All applicant organizations must register with Grants.gov. Please visit www.Grants.gov at least 30 days prior to submitting your application to familiarize yourself with the registration and submission processes. The "one-time" registration process will take three to five days to complete. However, it is best to start the registration process at least two weeks prior to application submission.

All Program Directors/Principal Investigators (PD/PIs) must also work with their institutional officials to register with the eRA Commons or ensure their existing Principle Investigator (PD/PI) eRA Commons account is affiliated with the eRA commons account of the applicant organization. All registrations must be successfully completed and active before the application due date. Applicant organizations are strongly encouraged to start the eRA Commons registration process at least four (4) weeks prior to the application due date. ASSIST requires that applicant users have active eRA Commons account in order to prepare an application. It also requires that the applicant organization's Signing Official have an active eRA Commons Signing Official account in order to initiate the submission process. During the submission process, ASSIST will prompt the Signing Official to enter their Grants.gov Authorized Organizational Representative (AOR) credentials in order to complete the submission, therefore the applicant organization must ensure that their Grants.gov AOR credentials are active.

7. Universal Identifier Requirements and System for Award Management (SAM)

All applicant organizations **must obtain** a DUN and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for Federal grants or cooperative agreements. The DUNS number is a nine-digit number assigned by Dun and Bradstreet Information Services. An AOR should be consulted to determine the appropriate number. If the organization does not have a DUNS number, an AOR should complete the US D&B D-U-N-S Number Request Web Form or contact Dun and Bradstreet by telephone directly at 1-866-705-5711 (toll-free) to obtain one. A DUNS number will be provided immediately by telephone at no charge. Note this is an organizational number. Individual

Program Directors/Principal Investigators do not need to register for a DUNS number. Additionally, all applicant organizations must register in the **System for Award Management (SAM)**. Organizations must maintain the registration with current information at all times during which it has an application under consideration for funding by CDC and, if an award is made, until a final financial report is submitted or the final payment is received, whichever is later. SAM is the primary registrant database for the Federal government and is the repository into which an entity must provide information required for the conduct of business as a recipient. Additional information about registration procedures may be found at the SAM internet site at https://www.sam.gov/index.html.
If an award is granted, the recipient organization **must** notify potential sub-recipients that no organization may receive a subaward under the grant unless the organization has provided its DUNS number to the recipient organization.

8. Eligible Individuals (Project Director/Principal Investigator) in Organizations/Institutions

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Project Director/Principal Investigator (PD/PI) is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for HHS/CDC support.

9. Cost Sharing

This FOA does not require cost sharing as defined in the HHS Grants Policy Statement (http://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf).

10. Number of Applications

As defined in the HHS Grants Policy Statement, (https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf), applications received in response to the same Notice of Funding Opportunity generally are scored individually and then ranked with other applications under peer review in their order of relative programmatic, technical, or scientific merit. HHS/CDC will not accept any application in response to this NOFO that is essentially the same as one currently pending initial peer review unless the applicant withdraws the pending application.

As defined in the HHS Grants Policy Statement,(https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf), applications received in response to the same Notice of Funding Opportunity generally are scored individually and then ranked with other applications under peer review in their order of relative programmatic, technical, or scientific merit. HHS/CDC will not accept any application in response to this NOFO that is essentially the same as one currently pending initial peer review unless the applicant withdraws the pending application.

Applicant institutions may not submit applications with the same, or similar, proposed research to two or more funding opportunities from CDC. Eligible applicant organizations may submit more than one application to this NOFO, provided that each application is scientifically distinct. However, applicant institutions can submit only one application with the same principal investigator. Only one application per principal investigator will be funded

under this announcement. If two or more applications from the same PI are received, the only application that will be submitted for review will be the first application received based on the time and date stamp for submission in Grants.gov .(http://www.grants.gov).

Section IV. Application and Submission Information

1. Address to Request Application Package

In order to use ASSIST, applicants must visit https://public.era.nih.gov/assist where you can login using your eRA Commons credentials, and enter the Notice of Funding Opportunity Number to initiate the application, and begin the application preparation process.
If you experience problems accessing or using ASSIST, you can refer to the ASSIST Online Help Site at: https://era.nih.gov/erahelp/assist. Additional support is available from the NIH eRA Service desk via:

- E-mail: http://grants.nih.gov/support/index.html
- Phone: 301-402-7469 or (toll-free) 1-866-504-9552. The NIH eRA Service desk is available Monday - Friday, 7 a.m. to 8 p.m. Eastern Time, excluding federal holidays.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the SF-424 (R&R) Application Guide http://grants.nih.gov/grants/how-to-apply-application-guide.htm and here: https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general-forms-e.pdf, except where instructed in this Notice of Funding Opportunity to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review. The package associated with this NOFO includes all applicable mandatory and optional forms. Please note that some forms marked optional in the application package are required for submission of applications for this NOFO. Follow the instructions in the SF-424 (R&R) Application Guide to ensure you complete all appropriate “optional” components.
When using ASSIST, all mandatory forms will appear as separate tabs at the top of the Application Information screen; applicants may add optional forms available for the NOFO by selecting the Add Optional Form button in the left navigation panel.

3. Letter of Intent

Due Date for Letter of Intent: **05/03/2019**

The Letter of Intent (LOI) is not required, but it helps us to plan and relegate appropriate resources for the Peer Review process.

Prospective applicants are asked to submit a letter of intent that includes the following information:

- contact information (name, title, address, phone, E-mail, etc.)
- affiliation

- NOFO number
- key personnel list
- a brief description of your intended research or proposed investigation and
- a positive statement of your intent to apply for a grant under this NOFO

The letter of intent should be sent to:

Mikel Walters, PhD

Scientific Review Officer for RFA-TS-19-002
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention (CDC)
4770 Buford Hwy, NE, Mailstop F-63
Atlanta, GA 30341
Telephone: 404-639-0913 Email: mwalters@cdc.gov

4. Required and Optional Components

A complete application has many components, both required and optional. The forms package associated with this NOFO in Grants.gov includes all applicable components for this NOFO, required and optional. In ASSIST, all required and optional forms will appear as separate tabs at the top of the Application Information screen.

5. PHS 398 Research Plan Component

The SF424 (R&R) Application Guide includes instructions for applicants to complete a PHS 398 Research Plan that consists of components. Not all components of the Research Plan apply to all Notices of Funding Opportunities (NOFOs). Specifically, some of the following components are for Resubmissions or Revisions only. See the SF 424 (R&R) Application Guide https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/generalforms-e.pdf and https://apply07.grants.gov/apply/forms/sample/SF424B-V1.1.pdf for additional information. Please attach applicable sections of the following Research Plan components as directed in Part 2, Section 1 (Notice of Funding Opportunity Description).
Follow the page limits stated in the SF 424 unless otherwise specified in the NOFO. As applicable to and specified in the NOFO, the application should include the bolded headers in this section and should address activities to be conducted over the course of the entire project, including but not limited to:

1. Introduction to Application (for Resubmission and Revision ONLY) - provide a clear description about the purpose of the proposed research and how it addresses the specific requirements of the NOFO.
2. Specific Aims – state the problem the proposed research addresses and how it will result in public health impact and improvements in population health.
3. Research Strategy – the research strategy should be organized under 3 headings: Significance, Innovation and Approach. Describe the proposed research plan, including staffing and time line.
4. Progress Report Publication List (for Continuation ONLY)

Other Research Plan Sections

5. **Vertebrate Animals**
6. **Select Agent Research**
7. **Multiple PD/PI Leadership Plan.**
8. **Consortium/Contractual Arrangements**
9. **Letters of Support**
10. **Resource Sharing Plan(s)**
11. **Authentication of Key Biological and/or Chemical Resources**
12. **Appendix**

All instructions in the SF424 (R&R) Application Guide https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general-forms-e.pdf and here: https://apply07.grants.gov/apply/forms/sample/SF424B-V1.1.pdf must be followed along with any additional instructions provided in the NOFO.
Applicants that plan to collect public health data must submit a Data Management Plan (DMP) in the Resource Sharing Plan section of the PHS 398 Research Plan Component of the application. A DMP is required for each collection of public health data proposed. Applicants who contend that the public health data they collect or create are not appropriate for release must justify that contention in the DMP submitted with their application for CDC funds.
The DMP may be outlined in a narrative format or as a checklist but, at a minimum, should include:
• Descriptions of the data to be produced in the proposed project
• How access will be provided to the data (including provisions for protection of privacy, confidentiality, security, intellectual property, or other rights)
• Use of data standards that ensure all released data have appropriate documentation that describes the method of collection, what the data represent, and potential limitations for use
• Plans for archival and long-term preservation of the data, or explaining why long-term preservation and access cannot be justified
Examples of DMPs may be found here: University of California https://dmp.cdlib.org/, or USGS, http://www.usgs.gov/datamanagement/plan/dmplans.php

DATA MANAGEMENT PLAN

CDC/ATSDR policy requires that the public health data collected or generated using CDC/ATSDR funds should be made readily available for scientific communities and/or the public. Awardees who fail to release public health data in a timely fashion will be subject to procedures normally used to address lack of compliance (for example, reduction in funding, restriction of funds, or award termination) consistent with 45 CFR 74.62 or other authorities as appropriate.

CDC/ATSDR requires federal fund recipients for projects and programs that involve new data collection or generation to develop and submit a Data Management Plan (DMP) for each collection or generation of public health data undertaken as part of the award. For purposes of this notice, “public health data” means digitally recorded factual material commonly accepted in

the scientific community as a basis for public health findings, conclusions, and implementation.

This requirement ensures that CDC/ATSDR is in compliance with the following: Office of Management and Budget (OMB) memorandum titled "Open Data Policy–Managing Information as an Asset" (OMB M-13-13); Executive Order 13642 titled "Making Open and Machine Readable the New Default for Government Information"; and the Office of Science and Technology Policy (OSTP) memorandum titled "Increasing Access to the Results of Federally Funded Scientific Research" (OSTP Memo).

Additional Requirement-25: Data Management and Access https://www.cdc.gov/grants/additionalrequirements/ar-25.html outlines the components of a DMP and provides additional information for awardees regarding the requirements for data accessibility, storage, and preservation. The DMP should be developed during the project planning phase prior to the initiation of collecting or generating public health data and will be submitted with the application. The submitted DMP will be evaluated for completeness and quality at the time of submission.

A DMP should include, at a minimum, following information:

- A description of the data to be collected or generated in the proposed project;
- Standards to be used for the collected or generated data;
- Mechanisms for or limitations to providing access to and sharing of the data (include a description of provisions for the protection of privacy, confidentiality, security, intellectual property, or other rights).
- Use of data standards that ensure all released data have appropriate documentation that describes the method of collection, what the data represent, and potential limitations for use;
- Plans for archiving and long-term preservation of the data, or explaining why long-term preservation and access are not justified; and
- If applicants who contend that the public health data they collect or create are not appropriate for release, they must justify that contention in the DMP (for example, privacy and confidentiality considerations).

Applications submitted without the required DMP may be deemed ineligible for award unless submission of DMP is deferred to a later period depending on the type of award, in which case, funding restrictions may be imposed pending submission and evaluation.

The DMP is considered a living document that will require updates throughout the lifecycle of the project. Awardees should update their DMP to include any updates to the project's data collection and reflect progress or issues with planned data collection. The updates to DMP should be submitted as required for each reporting period. Awardees must include an updated final Data Management Plan that describes the data collected, the location of where the data is stored (example: a repository), accessibility restrictions (if applicable), and the plans for long term preservation of the data.

6. Appendix

Do not use the appendix to circumvent page limits. A maximum of 10 PDF documents are

allowed in the appendix. Additionally, up to 3 publications may be included that are not publically available. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

7. Page Limitations

All page limitations described in this individual NOFO must be followed. For this specific NOFO, the Research Strategy component of the Research Plan narrative is limited to 20 pages. Supporting materials for the Research Plan narrative included as appendices may not exceed 10 PDF files with a maximum of 50 pages for all appendices.

8. Format for Attachments

Designed to maximize system-conducted validations, multiple separate attachments are required for a complete application. When the application is received by the agency, all submitted forms and all separate attachments are combined into a single document that is used by peer reviewers and agency staff. Applicants should ensure that all attachments are uploaded to the system.
CDC requires all text attachments to the Adobe application forms be submitted as PDFs and that all text attachments conform to the agency-specific formatting requirements noted in the SF424 (R&R) Application Guide https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general-forms-e.pdf and here: https://apply07.grants.gov/apply/forms/sample/SF424B-V1.1.pdf.

9. Submission Dates & Times

Part I. Overview Information contains information about Key Dates. Applicants are strongly encouraged to allocate additional time and submit in advance of the deadline to ensure they have time to make any corrections that might be necessary for successful submission. This includes the time necessary to complete the application resubmission process that may be necessary, if errors are identified during validation by Grants.gov and the NIH eRA systems. The application package is not complete until it has passed the Grants.gov and NIH eRA Commons submission and validation processes.
Organizations must submit applications using the ASSIST web-based application preparation and submission process.
ASSIST will validate applications before submission. If the system detects errors, then the applicant must correct errors before their application can be submitted.
Applicants are responsible for viewing their application in ASSIST after submission to ensure accurate and successful submission through Grants.gov. If the submission is not successful and post-submission errors are found, then those errors must be corrected and the application resubmitted in ASSIST.
Applicants are able to access, view, and track the status of their applications in the eRA Commons.
Information on the submission process is provided in the SF-424 (R&R) Application Guidance and ASSIST User Guide at https://era.nih.gov/files/ASSIST_user_guide.pdf.
Note: HHS/CDC grant submission procedures do not provide a grace period beyond the grant application due date time to correct any error or warning notices of noncompliance with application instructions that are identified by Grants.gov or eRA systems (i.e. error correction window).

Applicants who encounter problems when submitting their applications must attempt to resolve them by contacting the NIH eRA Service desk at:
Toll-free: 1-866-504-9552; Phone: 301-402-7469
http://grants.nih.gov/support/index.html
Hours: Mon-Fri, 7 a.m. to 8 p.m. Eastern Time (closed on federal holidays)

Problems with Grants.gov can be resolved by contacting the Grants.gov Contact Center at:
Toll-free: 1-800-518-4726
https://www.grants.gov/web/grants/support.html
support@grants.gov
Hours: 24 hours a day, 7 days a week (closed on federal holidays)
If the applicant encounters problems that prevent the ability to submit an application which cannot be resolved by Grants.gov or NIH eRA Service Desks, then applicants must contact CDC Technical Information Management Section (TIMS) at 770-488-2700; ogstims@cdc.gov for guidance at least 3 calendar days before the deadline date. Therefore, it is important that applicants complete the application submission process well in advance of the due date time.
After submission of your application package, applicants will receive a "submission receipt" email generated by Grants.gov. Grants.gov will then generate a second e-mail message to applicants which will either validate or reject their submitted application package. A third and final e-mail message is generated once the applicant's application package has passed validation and the grantor agency has confirmed receipt of the application.

Unsuccessful Submissions: If an application submission was unsuccessful, the **applicant** must:

1. Track submission and verify the submission status (tracking should be done initially regardless of rejection or success).

    a. If the status states "**rejected**", do #2a or #2b

2. Check emails from both Grants.gov and NIH eRA Commons for rejection notices.

    a. If the deadline has passed, he/she should email the Grants Management contact listed in the Agency Contacts section of this announcement and ogstims@cdc.gov explaining why the submission failed.
    b. If there is time before the deadline, correct the problem(s) and resubmit as soon as possible.

Due Date for Applications: **06/03/2019**

Electronically submitted applications must be submitted no later than 5:00 p.m., ET, on the listed application due date.

10. Intergovernmental Review (E.O. 12372)

Your application is subject to Intergovernmental Review of Federal Programs, as governed by Executive Order 12372 (http://www.archives.gov/federal-register/codification/executive-

order/12372.html). This order sets up a system for state and local review of proposed federal assistance applications. You should contact your state single point of contact (SPOC) as early as possible to alert the SPOC to prospective applications, and to receive instructions on your state's process. Click on the following link to get the current SPOC list: https://www.whitehouse.gov/wp-content/uploads/2017/11/Intergovernmental_-Review-_SPOC_01_2018_OFFM.pdf.

11. Funding Restrictions

All HHS/CDC awards are subject to the federal regulations, 45 CFR 75, terms and conditions, and other requirements described in the HHS Grants Policy Statement. Pre-award costs may be allowable as an expanded authority, but only if authorized by CDC.

In accordance with the United States Protecting Life in Global Health Assistance policy, all non-governmental organization (NGO) applicants acknowledge that foreign NGOs that receive funds provided through this award, either as a prime recipient or subrecipient, are strictly prohibited, regardless of the source of funds, from performing abortions as a method of family planning or engaging in any activity that promotes abortion as a method of family planning, or to provide financial support to any other foreign non-governmental organization that conducts such activities. See Additional Requirement (AR) 35 for applicability (https://www.cdc.gov/grants/additionalrequirements/ar-35.html).

For more information on expanded authority and pre-award costs, go to: https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf.

CDC requires that mechanisms for, and cost of, public health data sharing be included in grants, cooperative agreements, and contracts. The cost of sharing or archiving public health data may also be included as part of the total budget requested for first-time or continuation awards. Fulfilling the data-sharing requirement must be documented in a Data Management Plan (DMP) that is developed during the project planning phase prior to the initiation of generating or collecting public health data and must be included in the Resource Sharing Plan(s) section of the PHS398 Research Plan Component of the application.

Applicants who contend that the public health data they collect or create are not appropriate for release must justify that contention in the DMP submitted with their application for CDC funds (for example, privacy and confidentiality considerations, embargo issues).

Recipients who fail to release public health data in a timely fashion will be subject to procedures normally used to address lack of compliance (for example, reduction in funding, restriction of funds, or award termination) consistent with 45 CFR 74.62 or other authorities as appropriate. For further information, please see: https://www.cdc.gov/grants/additionalrequirements/ar-25.html for revised AR-25.

12. Other Submission Requirements and Information

Risk Assessment Questionnaire Requirement

CDC is required to conduct pre-award risk assessments to determine the risk an applicant poses to meeting federal programmatic and administrative requirements by taking into account issues such as financial instability, insufficient management systems, non-compliance with award conditions, the charging of unallowable costs, and inexperience. The risk assessment will

include an evaluation of the applicant's CDC Risk Questionnaire, located at https://www.cdc.gov/grants/documents/PPMR-G-CDC-Risk-Questionnaire.pdf, as well as a review of the applicant's history in all available systems; including OMB-designated repositories of government-wide eligibility and financial integrity systems (see 45 CFR 75.205(a)), and other sources of historical information. These systems include, but are not limited to: FAPIIS (https://www.fapiis.gov/), including past performance on federal contracts as per Duncan Hunter National Defense Authorization Act of 2009; Do Not Pay list; and System for Award Management (SAM) exclusions.
CDC requires all applicants to complete the Risk Questionnaire, OMB Control Number 0920-1132 annually. This questionnaire, which is located at https://www.cdc.gov/grants/documents/PPMR-G-CDC-Risk-Questionnaire.pdf, along with supporting documentation must be submitted with your application by the closing date of the Notice of Funding Opportunity Announcement. If your organization has completed CDC's Risk Questionnaire within the past 12 months of the closing date of this NOFO, then you must submit a copy of that questionnaire, or submit a letter signed by the authorized organization representative to include the original submission date, organization's EIN and DUNS.

When uploading supporting documentation for the Risk Questionnaire into this application package, clearly label the documents for easy identification of the type of documentation. For example, a copy of Procurement policy submitted in response to the questionnaire may be labeled using the following format: Risk Questionnaire Supporting Documents _ Procurement Policy.

Duplication of Efforts
Applicants are responsible for reporting if this application will result in programmatic, budgetary, or commitment overlap with another application or award (i.e. grant, cooperative agreement, or contract) submitted to another funding source in the same fiscal year. Programmatic overlap occurs when (1) substantially the same project is proposed in more than one application or is submitted to two or more funding sources for review and funding consideration or (2) a specific objective and the project design for accomplishing the objective are the same or closely related in two or more applications or awards, regardless of the funding source. Budgetary overlap occurs when duplicate or equivalent budgetary items (e.g., equipment, salaries) are requested in an application but already are provided by another source. Commitment overlap occurs when an individual's time commitment exceeds 100 percent, whether or not salary support is requested in the application. Overlap, whether programmatic, budgetary, or commitment of an individual's effort greater than 100 percent, is not permitted. Any overlap will be resolved by the CDC with the applicant and the PD/PI prior to award. Report Submission: The applicant must upload the report under "Other Attachment Forms." The document should be labeled: "Report on Programmatic, Budgetary, and Commitment Overlap."

Application Submission
Applications must be submitted electronically following the instructions described in the SF 424 (R&R) Application Guide. **PAPER APPLICATIONS WILL NOT BE ACCEPTED.**

Applicants must complete all required registrations before the application due date. Section III.6 "Required Registrations" contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically (http://grants.nih.gov/grants/guide /url_ redirect.htm? id=11144).

Important reminders:
All PD/PIs must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF 424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to CDC.
The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management (SAM). Additional information may be found in the SF424 (R&R) Application Guide.
If the applicant has an FWA number, enter the 8-digit number. Do not enter the letters "FWA" before the number. If a Project/Performance Site is engaged in research involving human subjects, the applicant organization is responsible for ensuring that the Project/Performance Site operates under and appropriate Federal Wide Assurance for the protection of human subjects and complies with 45 CFR Part 46 and other CDC human subject related policies described in Part II of the SF 424 (R&R) Application Guide and in the HHS Grants Policy Statement.

See more resources to avoid common errors and submitting, tracking, and viewing applications:

- http://grants.nih.gov/grants/ElectronicReceipt/avoiding_errors.htm
- http://grants.nih.gov/grants/ElectronicReceipt/submit_app.htm
- https://era.nih.gov/files/ASSIST_user_guide.pdf
- http://era.nih.gov/erahelp/ASSIST/

Upon receipt, applications will be evaluated for completeness by the CDC Office of Grants Services (OGS) and responsiveness by OGS and the Center, Institute or Office of the CDC. Applications that are incomplete and/or nonresponsive will not be reviewed.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. As part of the CDC mission (http:// www.cdc.gov/ about/ organization/ mission.htm), all applications submitted to the CDC in support of public health research are evaluated for scientific and

technical merit through the CDC peer review system.

Overall Impact
Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the project proposed).

Scored Review Criteria
Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

i. Approach

Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Does the applicant address the research objectives as stated in Section I of the NOFO? Does the proposed study protocol contain all the necessary elements mentioned in the sample ATSDR protocol (current draft available at https://www.atsdr.cdc.gov/PFAS/PFAS-Research-NOFO.html) ? Does the applicant propose using a rigorous experimental design that includes data analytic plans appropriate to the research design and hypotheses? Does the applicant demonstrate the ability to access the necessary data to execute the research plan? Are these data appropriate for the research? Does the applicant propose a study with adequate sample size to test the proposed hypotheses? Do the proposed data collection methods adequately represent the anticipated general core activities for data collection listed in the NOFO? Does the applicant demonstrate an understanding of the source(s) of the PFAS contamination of drinking water? Does the applicant provide information on the data sources and methods that will be used to historically reconstruct the PFAS concentrations in the drinking water? If the site is served by a public water system, does the applicant provide information on the characteristics of the system? If the site is served by private wells, does the applicant provide information on the extent of the contamination (e.g., delineation of the groundwater contaminant plume, number of wells affected)?

ii. Evaluation and Performance Measurement

Are the PD/PIs, collaborators, and other researchers well suited to the project? Have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

Does the application include adequate information on the project team's experience in conducting research consistent with that proposed in the application's research plan? Does the

application's analytic plans effectively describe the research design and hypotheses, data collection measures, and methods to evaluate whether the proposed research plan can effectively address the proposed hypotheses? Are the outcomes to be evaluated clearly specified?

iii. Applicant's Organizational Capacity to Implement the Approach

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Does the application include adequate information on the project team's experience in conducting research consistent with that proposed in the application's research plan? Is the proposed research outside of the cor activities innovative and yet offer a reasonable potential of meeting the Purpose and Research Objectives of this NOFO? Does the application demonstrate the organizational capacity elements listed in the NOFO? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Does the applicant demonstrate the ability to access the necessary data to execute the research plan?

Budget

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed?
If the project involves clinical research, are there plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

Does the applicant organization clearly demonstrate that it will conduct a substantial portion of the research plan, including a proposed budget that does not reflect an intent to act as a "pass through" organization for partner entities? Do the submitted letters of support or memoranda of understanding clearly describe the working relationships between the research institution and all partner organizations? Is the nature of and extent of each entity's involvement sufficient for the successful completion of the proposed research project as a whole?

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of

the scientific environment, subject populations, or collaborative arrangements? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Are the partnerships necessary and critical for the successful completion of the proposed project documented in the application by letters of support or memoranda of understanding that include detailed information about the nature of existing relationships?

2. Additional Review Criteria

As applicable for the project proposed, *reviewers will evaluate* the following additional items while determining scientific and technical merit, and in providing an overall impact/priority score, but *will not give separate scores* for these items.

Protections for Human Subjects

If the research involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the HHS/CDC Requirements under AR-1 Human Subjects Requirements (https://www.cdc.gov/grants/additionalrequirements/ar-1.html).

If your proposed research involves the use of human data and/or biological specimens, you must provide a justification for your claim that no human subjects are involved in the Protection of Human Subjects section of the Research Plan.

Inclusion of Women, Minorities, and Children

When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children. For additional information on review of the Inclusion section, please refer to the policy on the Inclusion of Women and Racial and Ethnic Minorities in Research (https://www.cdc.gov/maso/Policy/Policy_women.pdf and the policy on the Inclusion of Persons Under 21 in Research (https://www.cdc.gov/maso/Policy/policy496.pdf).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and

tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (https://grants.nih.gov/grants/olaw/VAChecklist.pdf).

Biohazards
Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Dual Use Research of Concern
Reviewers will identify whether the project involves one of the agents or toxins described in the US Government Policy for the Institutional Oversight of Life Sciences Dual Use Research of Concern, and, if so, whether the applicant has identified an IRE to assess the project for DURC potential and develop mitigation strategies if needed.

For more information about this Policy and other policies regarding dual use research of concern, visit the U.S. Government Science, Safety, Security (S3) website at: http://www.phe.gov/s3/dualuse. Tools and guidance for assessing DURC potential may be found at: http://www.phe.gov/s3/dualuse/Pages/companion-guide.aspx.

3. Additional Review Considerations

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact/priority score.

- Will undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review), will be discussed and assigned an overall impact/priority score.

Resource Sharing Plan(s)
HHS/CDC policy requires that recipients of grant awards make research resources and data readily available for research purposes to qualified individuals within the scientific community after publication. Please see: https://www.cdc.gov/grants/additionalrequirements/ar-25.html

New additional requirement: CDC requires recipients for projects and programs that involve data collection or generation of data with federal funds to develop and submit a Data Management Plan (DMP) for each collection of public health data.

Investigators responding to this Notice of Funding Opportunity should include a detailed DMP in the Resource Sharing Plan(s) section of the PHS 398 Research Plan Component of the application. The AR-25 outlines the components of a DMP and provides additional information for investigators regarding the requirements for data accessibility,

storage, and preservation.

The DMP should be developed during the project planning phase prior to the initiation of collecting or generating public health data and will be submitted with the application. The submitted DMP will be evaluated for completeness and quality at the time of submission.

The DMP should include, at a minimum, a description of the following:

• Type of data to be produced in the proposed project;
• Mechanisms for providing access to and sharing of the data (including provisions for the protection of privacy, confidentiality, security, intellectual property, or other rights);
• Use of data standards that ensure all released data have appropriate documentation that describes the method of collection, what the data represent, and potential limitations for use; and
• Plans for archiving and long-term preservation of the data, or explaining why long-term preservation and access are not justified.

Applications submitted without the required DMP may be deemed ineligible for award unless submission of DMP is deferred to a later period depending on the type of award, in which case, funding restrictions may be imposed pending submission and evaluation.

Budget and Period of Support
Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research. The applicant can obtain guidance for completing a detailed justified budget on the CDC website, at the following Internet address: http://www.cdc.gov/grants/interestedinapplying/applicationresources.html
The budget can include both direct costs and indirect costs as allowed.
Indirect costs could include the cost of collecting, managing, sharing and preserving data.
Indirect costs on grants awarded to foreign organizations and foreign public entities and performed fully outside of the territorial limits of the U.S. may be paid to support the costs of compliance with federal requirements at a fixed rate of eight percent of modified total direct costs exclusive of tuition and related fees, direct expenditures for equipment, and subawards in excess of $25,000. Negotiated indirect costs may be paid to the American University, Beirut, and the World Health Organization.
Indirect costs on training grants are limited to a fixed rate of eight percent of MTDC exclusive of tuition and related fees, direct expenditures for equipment, and sub-awards in excess of $25,000.
If requesting indirect costs in the budget based on a federally negotiated rate, a copy of the indirect cost rate agreement is required. Include a copy of the current negotiated federal indirect cost rate agreement or cost allocation plan approval letter.

4. Review and Selection Process

Applications will be evaluated for scientific and technical merit by an appropriate peer review group, in accordance with CDC peer review policy and procedures, using the stated review criteria.

As part of the scientific peer review, all applications:

The following will be considered in making funding decisions of the proposed research project as determined by scientific peer review:

- Source(s) of contamination
- PFAS concentrations at the tap(s) at the selected study site(s)
- Proposed method for historical reconstruction of drinking water PFAS concentrations, including methods/models and data sources
- Geographic Balance of proposed projects

- Will receive a written critique.

Applications will be assigned to the appropriate HHS/CDC Center, Institute, or Office. Applications will compete for available funds with all other recommended applications submitted in response to this NOFO. Following initial peer review, recommended applications will receive a second level of review. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

5. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) and other pertinent information via the eRA Commons.

Section VI. Award Administration Information

1. Award Notices

Any applications awarded in response to this NOFO will be subject to the DUNS, SAM Registration, and Transparency Act requirements. If the application is under consideration for funding, HHS/CDC will request "just-in-time" information from the applicant as described in the HHS Grants Policy Statement (https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the Grants Management Officer is the authorizing document and will be sent via email to the grantee's business official.

Recipient must comply with any funding restrictions as described in Section IV.11. Funding Restrictions. Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be allowable as an expanded authority, but only if authorized by CDC.

2. CDC Administrative Requirements

Overview of Terms and Conditions of Award and Requirements for Specific Types of Grants

Administrative and National Policy Requirements, Additional Requirements (ARs) outline the administrative requirements found in 45 CFR Part 75 and the HHS Grants Policy Statement and other requirements as mandated by statute or CDC policy. Recipients must comply with administrative and national policy requirements as appropriate. For more information on the Code of Federal Regulations, visit the National Archives and Records Administration: http://www.access.gpo.gov/nara/cfr/cfr-table- search.html.

Specific requirements that apply to this NOFO are the following:

AR-1: Human Subjects Requirements

AR-2: Requirements for Inclusion of Women and Racial and Ethnic Minorities in Research

AR-7: Executive Order 12372 Review

AR-9: Paperwork Reduction Act Requirements

AR-10: Smoke-Free Workplace Requirements

AR-11: Healthy People 2020

AR-12: Lobbying Restrictions

AR-13: Prohibition on Use of CDC Funds for Certain Gun Control Activities

AR-14: Accounting System Requirements

AR-16: Security Clearance Requirement

AR-19: Third Party Agreements – ATSDR (AR-19)

AR-21: Small, Minority, And Women-owned Business

AR-22: Research Integrity

AR-24: Health Insurance Portability and Accountability Act Requirements

AR-25: Data Management and Access

AR-26: National Historic Preservation Act of 1966

AR-28: Inclusion of Persons Under the Age of 21 in Research

AR-29: Compliance with EO13513, “Federal Leadership on Reducing Text Messaging while Driving”, October 1, 2009

AR-30: Information Letter 10-006, - Compliance with Section 508 of the Rehabilitation Act of 1973

AR-31: Research Definition

AR-32: Appropriations Act, General Provisions

AR-33: United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern

AR-34: Language Access for Persons with Limited English Proficiency

AR-36: ; Certificates of Confidentiality

Paperwork Reduction Act / Information Collection:

Applicants are advised that any activities involving information collection (i.e., posting similar questions or requirements via surveys, questionnaires, telephonic requests, focus groups, etc.) from 10 or more non-Federal entities/persons, including states, are subject to Paperwork Reduction Act (PRA) requirements and may or may not be subject to approval by the Office of Management and Budget (OMB) under the Paperwork Reduction Act (PRA) prior to the start of information collection activities. PRA applicability will depend on the level of CDC involvement with the development, collection, and management of information/data.

CDC Assurances and Certifications:

All applicants are required to sign and submit "Assurances and Certifications" documents indicated at http://www.cdc.gov/od/pgo/funding/grants/foamain.shtm.
Applicants may follow either of the following processes:

- Complete the applicable assurances and certifications on an annual basis, name the file "Assurances and Certifications" and upload it as a PDF file at www.grants.gov or
- Complete the applicable assurances and certifications and submit them directly to CDC on an annual basis at:
  http://wwwn.cdc.gov/grantassurances/(S(mj444mxct51lnrv1hljjjmaa))/Homepage.asp

Assurances and certifications submitted directly to CDC will be kept on file for one year and will apply to all applications submitted to CDC by the applicant within one year of the submission date.

Changes to Certificate of Confidentiality (CoC)

1. All Certificates of Confidentiality (CoC)s issued in the past or in the future by the CDC, must comply with the new requirements of subsection 301(d) of the Public Health Service Act as amended, especially the new disclosure requirements and restrictions.
    a. The new disclosure requirements prohibit disclosure of the name of research subjects or any identifiable research information, document, or biospecimen to anyone not connected with the research except under very specific circumstances including:

    - If required by other Federal, State, or local laws, such as for reporting of communicable diseases;

    - If the subject consents;

    - Or for the purposes of scientific research that is compliant with human subjects

regulations.

2. For studies in which informed consent is sought, CDC expects investigators to inform research participants of the new protections and the limits to protections provided by a CoC. CoCs will now automatically cover any CDC-funded project collecting or using identifiable, sensitive information that was new or on-going as of December 13, 2016.

- The CoC will apply as a term and condition of award
- There will be no physical certificate issued

3. Automatic coverage of a CoC means that institutions and investigators do not need to apply for a CoC. However, institutions and investigators are responsible for determining whether research they conduct is subject to subsection 301(d) of the Public Health Service Act.

3. Additional Policy Requirements

The following are additional policy requirements relevant to this NOFO:

HHS Policy on Promoting Efficient Spending: Use of Appropriated Funds for Conferences and Meetings, Food, Promotional Items and Printing Publications This policy supports the Executive Order on Promoting Efficient Spending (EO 13589), the Executive Order on Delivering and Efficient, Effective, and Accountable Government (EO 13576) and the Office of Management and Budget Memorandum on Eliminating Excess Conference Spending and Promoting Efficiency in Government (M-35-11). This policy apply to all new obligations and all funds appropriated by Congress. For more information, visit the HHS website at: https://www.hhs.gov/grants/contracts/contract-policies-regulations/efficient-spending/index.html.

Federal Funding Accountability and Transparency Act of 2006 Federal Funding Accountability and Transparency Act of 2006 (FFATA), P.L. 109–282, as amended by section 6202 of P.L. 110–252, requires full disclosure of all entities and organizations receiving Federal funds including grants, contracts, loans and other assistance and payments through a single, publicly accessible website, www.usaspending.gov. For the full text of the requirements, please review the following website: https://www.fsrs.gov/.

Plain Writing Act The Plain Writing Act of 2010, Public Law 111-274 was signed into law on October 13, 2010. The law requires that federal agencies use "clear Government communication that the public can understand and use" and requires the federal government to write all new publications, forms, and publicly distributed documents in a "clear, concise, well-organized" manner. For more information on this law, go to: http://www.plainlanguage.gov/plLaw/index.cfm.

Pilot Program for Enhancement of Employee Whistleblower Protections All applicants will be subject to a term and condition that applies the terms of 48 CFR section 3.908 to the award and requires that grantees inform their employees in writing (in the predominant native language of the workforce) of employee whistleblower rights and protections under 41 U.S.C. 4712.

Copyright Interests Provision This provision is intended to ensure that the public has access to the results and accomplishments of public health activities funded by CDC. Pursuant to

applicable grant regulations and CDC's Public Access Policy, Recipient agrees to submit into the National Institutes of Health (NIH) Manuscript Submission (NIHMS) system an electronic version of the final, peer-reviewed manuscript of any such work developed under this award upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. Also at the time of submission, Recipient and/or the Recipient's submitting author must specify the date the final manuscript will be publicly accessible through PubMed Central (PMC). Recipient and/or Recipient's submitting author must also post the manuscript through PMC within twelve (12) months of the publisher's official date of final publication; however the author is strongly encouraged to make the subject manuscript available as soon as possible. The recipient must obtain prior approval from the CDC for any exception to this provision.
The author's final, peer-reviewed manuscript is defined as the final version accepted for journal publication, and includes all modifications from the publishing peer review process, and all graphics and supplemental material associated with the article. Recipient and its submitting authors working under this award are responsible for ensuring that any publishing or copyright agreements concerning submitted articles reserve adequate right to fully comply with this provision and the license reserved by CDC. The manuscript will be hosted in both PMC and the CDC Stacks institutional repository system. In progress reports for this award, recipient must identify publications subject to the CDC Public Access Policy by using the applicable NIHMS identification number for up to three (3) months after the publication date and the PubMed Central identification number (PMCID) thereafter.

Language Access for Persons with Limited English Proficiency Recipients of federal financial assistance from HHS must administer their programs in compliance with federal civil rights law. This means that recipients of HHS funds must ensure equal access to their programs without regard to a person's race, color, national origin, disability, age and, in some circumstances, sex and religion. This includes ensuring your programs are accessible to persons with limited English proficiency. Recipients of federal financial assistance must take the reasonable steps to provide meaningful access to their programs by persons with limited English proficiency.

Dual Use Research of Concern On September 24, 2014, the US Government Policy for the Institutional Oversight of Life Sciences Dual Use Research of Concern was released. Grantees (foreign and domestic) receiving CDC funding on or after September 24, 2015 are subject to this policy. Research funded by CDC involving the agents or toxins named in the policy, must be reviewed to determine if it involves one or more of the listed experimental effects and if so, whether it meets the definition of DURC. This review must be completed by an Institutional Review Entity (IRE) identified by the funded institution.

Recipients also must establish an Institutional Contact for Dual Use Research (ICDUR). The award recipient must maintain records of institutional DURC reviews and completed risk mitigation plans for the term of the research grant, cooperative agreement or contract plus three years after its completion, but no less than eight years, unless a shorter period is required by law or regulation.

If a project is determined to be DURC, a risk/benefit analysis must be completed. CDC will work collaboratively with the award recipient to develop a risk mitigation plan that the CDC must

approve. The USG policy can be found at http://www.phe.gov/s3/dualuse.

Non-compliance with this Policy may result in suspension, limitation, restriction or termination of USG funding, or loss of future USG funding opportunities for the non-compliant USG-funded research project and of USG funds for other life sciences research at the institution, consistent with existing regulations and policies governing USG funded research, and may subject the institution to other potential penalties under applicable laws and regulations.

Data Management Plan(s)
CDC requires that all new collections of public health data include a Data Management Plan (DMP). For purposes of this announcement, "public health data" means digitally recorded factual material commonly accepted in the scientific community as a basis for public health findings, conclusions, and implementation.

This new requirement ensures that CDC is in compliance with the following; Office of Management and Budget (OMB) memorandum titled "Open Data Policy–Managing Information as an Asset" (OMB M-13-13); Executive Order 13642 titled "Making Open and Machine Readable the New Default for Government Information"; and the Office of Science and Technology Policy (OSTP) memorandum titled "Increasing Access to the Results of Federally Funded Scientific Research" (OSTP Memo).

The AR-25 https://www.cdc.gov/grants/additionalrequirements/ar-25.html outlines the components of a DMP and provides additional information for investigators regarding the requirements for data accessibility, storage, and preservation.
Certificates of Confidentiality: Institutions and investigators are responsible for determining whether research they conduct is subject to Section 301(d) of the Public Health Service (PHS) Act. Section 301(d), as amended by Section 2012 of the 21st Century Cures Act, P.L. 114-255 (42 U.S.C. 241(d)), states that the Secretary shall issue Certificates of Confidentiality (Certificates) to persons engaged in biomedical, behavioral, clinical, or other research activities in which identifiable, sensitive information is collected. In furtherance of this provision, CDC supported research commenced or ongoing after December 13, 2016 in which identifiable, sensitive information is collected, as defined by Section 301(d), is deemed issued a Certificate and therefore required to protect the privacy of individuals who are subjects of such research. Certificates issued in this manner will not be issued as a separate document, but are issued by application of this term and condition to this award. See Additional Requirement 36 to ensure compliance with this term and condition. The link to the full text is at: https://www.cdc.gov/grants/additionalrequirements/ar-36.html.

4. Cooperative Agreement Terms and Conditions

Applicant and CDC Role(s) in the Cooperative Agreement Research Project

Primary responsibilities of the PD(s)/PI(s):

- Collaborating with a single IRB to review and approve all non-exempt human subjects research activities conducted under this cooperative agreement.

- Participating in an initial kick-off meeting with CDC by phone or in Atlanta.
- Establishing an office at the study site to collect data from the study participants and to store biological samples.
- Complying with the responsibilities for extramural investigators for the Data Management and Access Additional Requirement (AR-25) described at: http://www.cdc.gov/grants/additional_requirements/index.html.
- Implementing the study procedures described in the ATSDR core protocol, including:
    - Establishing a community participatory mechanism (e.g., a community assistance panel or "CAP") to represent the interests and concerns of the study site community.
    - Enrollment of study participants, including determining eligibility, verifying their current contact information for results reporting, and potential future contact, and obtaining informed consent.
    - Recruitment of study participants.
- Data collection including:
    - Body and clinical measurements.
    - Administering questionnaire(s).
    - Ensuring that appropriately trained and credentialed staff administer the neurobehavioral tests.
    - Administering the neurobehavioral tests to each child and the parent.
    - Obtaining a fasting blood sample from each study participant.
    - Obtaining a first morning void urine sample from each study participant.
    - Ensuring retention of identifiable study participant contact information for future research.
    - Ensuring that appropriately trained and credentialed staff collect the blood samples.
    - Reimbursing study participants.
- Collecting and shipping PFAS samples to CDC/ATSDR for analysis.
- Collecting and shipping samples for clinical and biomarker testing to the ATSDR designated laboratory.
- Maintaining the security of the data collected, including any data and samples transmitted and/or shipped to ATSDR.*
- Maintaining quality control and integrity of the collected biological samples until delivered to the analyzing lab.
- Preparing monthly and quarterly progress reports for ATSDR staff's review.

Primary responsibilities of CDC/ATSDR staff:

- Schedule and conduct an initial kick-off meeting with the successful applicants.
- Provide the successful applicants with the final, approved ATSDR core study protocol and attachments, including consent forms and questionnaires.
- Provide technical assistance as requested by participating Stakeholders.
- Coordinate and provide guidance to recipients on sample transfer to ATSDR or an ATSDR-designated laboratory facility for analysis.
- Obtain CDC IRB and OMB approvals, as appropriate.
- Establish a secure share folder for the data that contains personal identifier information.
- Conduct laboratory analyses of PFAS in human serum samples submitted by successful applicants.
- Assist in the coordination, negotiation and implementation of an inter-laboratory comparability plan among all successful applicants for testing clinical outcomes.
- ATSDR may provide a data coordinating center to coordinate and house the data resulting from sample analysis (of the core activities) for all sites, and will provide individual site-specific data back to each site in addition to de-identified data collected from all sites.
- Monitor the progress of the study through conference calls, reviewing monthly and quarterly progress reports from the successful applicants, and performing site visits as necessary.
- Provide technical assistance as requested by the successful awardees to address and/or resolve conflicting issues, including Community Assistance Panel issues, that may arise at the different study sites.
- Collaborate in data analyses and manuscripts preparation for publication in scientific journals.

Areas of Joint Responsibility include:

Applicants and CDC staff intend to work collaboratively in the conduct of this multi-site research cooperative agreement. CDC/ATSDR intends to work with successful applicants on the following activities:

- Ensuring successful applicants follow the procedure to be used to submit samples to ATSDR and/or an ATSDR-designated laboratory for conducting analyses of clinical and research biomarkers (within the first 6 months post award).
- Coordinating PFAS sample collection, aliquoting, and transport (throughout the period of performance).
- Developing, conducting, and participating in a two-day community engagement PFAS summit in February, 2020 (tentative date) in Atlanta, GA. ATSDR will provide funding for travel, lodging, per diem, and transportation costs for this trip separate from the successful awardees' budgets. Each PI would be responsible for making their travel arrangements to attend this summit.
- Implementing appropriate quality assurance steps needed for data and biological sample collection.
- Implementing and remaining in compliance with human subjects protection and related

requirements.

- Preparing and submitting IRB and OMB approval packages, as appropriate.

Given the extent of ATSDR staff involvement in this research activity, it is anticipated that Office of Management and Budget (OMB) approval will be necessary before data collection can begin.

*Successful applicants who collect, store, process, transmit or use information on behalf of HHS or any of its component organizations may be subject to the requirements of the Federal Information Security Management Act (FISMA) in order for ATSDR to obtain the data from them. The extensive process that ATSDR will have to complete involves CDC/OCISSO requirements.

Common Rule Requirements

On September 8, 2015, the Department of Health and Human Services (HHS) and 15 other federal departments and agencies published a notice of proposed rulemaking (NPRM) proposing revisions to each agency's codification of the Federal Policy for the Protection of Human Subjects, originally promulgated as a Common Rule in 1991. On January 19, 2017, HHS and other federal departments and agencies published a final rule revising the Federal Policy for the Protection of Human Subjects. (82 FR 7149). https://www.federalregister.gov/documents/2017/01/19/2017-01058/federal-policy-for-the-protection-of-human-subjects

The 2018 Common Rule Update has new requirements for cooperative research at Title 45 Code of US Federal Regulations, Part 46, and creates a requirement for U.S.-based institutions engaged in cooperative research to use a single Institutional Review Board (IRB) for that portion of the research that takes place within the United States, with certain exceptions. https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&;SID=83cd09e1c0f5c6937cd9d7513160fc3f&;pitd=20180719&;n=pt45.1.46&;r=PART&;ty=HTML

Successful awardees under this cooperative agreement will be subject to the new rules, including the need to collaborate in selecting a single IRB to review and approve all non-exempt human subjects research activities conducted under this cooperative agreement.

5. Reporting

Recipients will be required to complete Research Performance Progress Report (RPPR) in eRA Commons at least annually (see https://grants.nih.gov/grants/rppr/index.htm; https://grants.nih.gov/grants/forms/report_on_grant.htm) and financial statements as required in the HHS Grants Policy Statement.

A final progress report, invention statement, equipment inventory list and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the HHS Grants Policy Statement.

Although the financial plans of the HHS/CDC CIO(s) provide support for this program, awards pursuant to this funding opportunity depend upon the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports) and the determination that continued funding is in the best interest of the Federal government.

The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for recipients of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later.
Compliance with this law is primarily the responsibility of the Federal agency. However, two elements of the law require information to be collected and reported by recipients:
1) Information on executive compensation when not already reported through the SAM Registration; and
2) Similar information on all sub-awards/ subcontracts/ consortiums over $25,000. It is a requirement for recipients of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All recipients of applicable CDC grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov on all subawards over $25,000. See the HHS Grants Policy Statement (https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf).

Successful applicants will prepare monthly and quarterly progress reports for ATSDR staff's review.

A. Submission of Reports
The Recipient Organization must provide HHS/CDC with an original, plus one hard copy of the following reports:

1. **Yearly Non-Competing Grant Progress Report**, is due 90 to 120 days before the end of the current budget period. The RPPR form (https://grants.nih.gov/grants/rppr/index.htm; https://grants.nih.gov/grants/rppr/rppr_instruction_guide.pdf) is to be completed on the eRA Commons website. The progress report will serve as the non-competing continuation application. Although the financial plans of the HHS/CDC CIO(s) provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports) and the determination that continued funding is in the best interest of the Federal government.

2. **Annual Federal Financial Report (FFR) SF 425** (https://grants.nih.gov/grants/forms/report_on_grant/federal_financial_report_ffr.htm) is required and must be submitted through eRA Commons **within 90 days after the end of the calendar quarter in which the budget period ends**.

3. **A final progress report**, invention statement, equipment/inventory report, and the final FFR are required **90 days after the end of the period of performance**.

B. Content of Reports

1. Yearly Non-Competing Grant Progress Report: The grantee's continuation

application/progress should include:

- Description of Progress during Annual Budget Period: Current Budget Period Progress reported on the RPPR form in eRA Commons (https://grants.nih.gov/grants/rppr/index.htm). Detailed narrative report for the current budget period that directly addresses progress towards the Measures of Effectiveness included in the current budget period proposal.
- Research Aims: list each research aim/project

a) Research Aim/Project: purpose, status (met, ongoing, and unmet), challenges, successes, and lessons learned
b) Leadership/Partnership: list project collaborations and describe the role of external partners.

- Translation of Research (1 page maximum). When relevant to the goals of the research project, the PI should describe how the significant findings may be used to promote, enhance, or advance translation of the research into practice or may be used to inform public health policy. This section should be understandable to a variety of audiences, including policy makers, practitioners, public health programs, healthcare institutions, professional organizations, community groups, researchers, and other potential users. The PI should identify the research findings that were translated into public health policy or practice and how the findings have been or may be adopted in public health settings. Or, if they cannot be applied yet, this section should address which research findings may be translated, how these findings can guide future research or related activities, and recommendations for translation. If relevant, describe how the results of this project could be generalized to populations and communities outside of the study. Questions to consider in preparing this section include:

- How will the scientific findings be translated into public health practice or inform public health policy?
- How will the project improve or effect the translation of research findings into public health practice or inform policy?
- How will the research findings help promote or accelerate the dissemination, implementation, or diffusion of improvements in public health programs or practices?
- How will the findings advance or guide future research efforts or related activities?

- Public Health Relevance and Impact (1 page maximum). This section should address improvements in public health as measured by documented or anticipated outcomes from the project. The PI should consider how the findings of the project relate beyond the immediate study to improved practices, prevention or intervention techniques, inform policy, or use of technology in public health. Questions to consider in preparing this section include:
- How will this project lead to improvements in public health?
- How will the findings, results, or recommendations been used to influence practices, procedures, methodologies, etc.?

- How will the findings, results, or recommendations contributed to documented or projected reductions in morbidity, mortality, injury, disability, or disease?

- Current Budget Period Financial Progress: Status of obligation of current budget period funds and an estimate of unobligated funds projected provided on an estimated FFR.

- New Budget Period Proposal:
- Detailed operational plan for continuing activities in the upcoming budget period, including updated Measures of Effectiveness for evaluating progress during the upcoming budget period. Report listed by Research Aim/Project.
- Project Timeline: Include planned milestones for the upcoming year (be specific and provide deadlines).

- New Budget Period Budget: Detailed line-item budget and budget justification for the new budget period. Use the CDC budget guideline format.

- Publications/Presentations: Include publications/presentations resulting from this CDC grant only during this budget period. If no publication or presentations have been made at this stage in the project, simply indicate "Not applicable: No publications or presentations have been made."

- IRB Approval Certification: Include all current IRB approvals to avoid a funding restriction on your award. If the research does not involve human subjects, then please state so. Please provide a copy of the most recent local IRB and CDC IRB, if applicable. If any approval is still pending at time of APR due date, indicate the status in your narrative.

- Update of Data Management Plan: The DMP is considered a living document that will require updates throughout the lifecycle of the project. Investigators should include any updates to the project's data collection such as changes to initial data collection plan, challenges with data collection, and recent data collected. Applicants should update their DMP to reflect progress or issues with planned data collection and submit as required for each reporting period.

- Additional Reporting Requirements:

Technical Review Statement Response Requirements

Grantees will be required to electronically submit a response to the peer reviewers' comments and/or concerns, as appropriate, within 30 days of the notification of their initial award. Grantees will also be required to electronically submit a response to any progress concerns or areas for improvement noted on their annual Technical Review, within the time period specified in the annual award continuation notice.

https://era.nih.gov/docs/Commons_UserGuide.pdf

2. Annual Federal Financial Reporting The Annual Federal Financial Report (FFR) SF 425 is required and must be submitted through eRA Commons within 90 days after the end of the calendar quarter in which the budget period ends. The FFR should only include those funds authorized and disbursed during the timeframe covered by the report. The final FFR must indicate the exact balance of unobligated funds and may not reflect any unliquidated obligations. There must be no discrepancies between the final FFR expenditure data and the Payment Management System's (PMS) cash transaction data.
Failure to submit the required information in a timely manner may adversely affect the future funding of this project. If the information cannot be provided by the due date, you are required to submit a letter explaining the reason and date by which the Grants Officer will receive the information.
The due date for final FFRs will continue to be 90 days after the Period of Performance end date. Recipients must submit closeout reports in a timely manner. Unless the Grants Management Officer (GMO) of the awarding Institute or Center approves an extension, recipients must submit a final FFR, final progress report, and Final Invention Statement and Certification within 90 days of the end of grant period. Failure to submit timely and accurate final reports may affect future funding to the organization or awards under the direction of the same Project Director/Principal Investigator (PD/PI).

FFR (SF 425) instructions for CDC recipients are now available at https://grants.nih.gov/grants/forms/report_on_grant/federal_financial_report_ffr.htm. For further information, contact GrantsInfo@nih.gov. Additional resources concerning the eFSR/FFR system, including a User Guide and an on-line demonstration, can be found on the eRA Commons Support Page: https://grants.nih.gov/support/index.html

FFR Submission: The submission of FFRs to CDC will require organizations to register with eRA Commons (Commons) (https:// commons. era.nih.gov/ commons/). CDC recommends that this one time registration process be completed at least 2 weeks prior to the submittal date of a FFR submission.

Organizations may verify their current registration status by running the "List of Commons Registered Organizations" query found at: https://era.nih.gov/registration_accounts.cfm. Organizations not yet registered can go to https://commons.era.nih.gov/commons for instructions. It generally takes several days to complete this registration process. This registration is independent of Grants.gov and may be done at any time.

The individual designated as the PI on the application must also be registered in the Commons. The PI must hold a PI account and be affiliated with the applicant organization. This registration must be done by an organizational official or their delegate who is already registered in the Commons. To register PIs in the Commons, refer to the eRA Commons User Guide found at: https://era.nih.gov/docs/Commons_UserGuide.pdf.

3. Final Reports: Final reports should provide sufficient detail for CDC to determine if the stated outcomes for the funded research have been achieved and if the research findings resulted in public health impact based on the investment. The grantee's final report should include:

- Research Aim/Project Overview: The PI should describe the purpose and approach to the project, including the outcomes, methodology and related analyses. Include a discussion of the challenges, successes and lessons learned. Describe the collaborations/partnerships and the role of each external partner.

- Translation of Research Findings: The PI should describe how the findings will be translated and how they will be used to inform policy or promote, enhance or advance the impact on public health practice. This section should be understandable to a variety of audiences, including policy makers, practitioners, public health programs, healthcare institutions, professional organizations, community groups, researchers and other potential end users. The PI should also provide a discussion of any research findings that informed policy or practice during the course of the period of performance. If applicable, describe how the findings could be generalized and scaled to populations and communities outside of the funded project.

- Public Health Relevance and Impact: This section should address improvements in public health as measured by documented or anticipated outcomes from the project. The PI should consider how the findings of the project related beyond the immediate study to improved practices, prevention or intervention techniques, or informed policy, technology or systems improvements in public health.

- Publications; Presentations; Media Coverage: Include information regarding all publications, presentations or media coverage resulting from this CDC funded activity. Please include any additional dissemination efforts that did or will result from the project.

- Final Data Management Plan: Applicants must include an updated final Data Management Plan that describes the data collected, the location of where the data is stored (example: a repository), accessibility restrictions (if applicable), and the plans for long term preservation of the data.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts
Grants.gov Customer Support (Questions regarding Grants.gov registration and submission, downloading or navigating forms)
Contact Center Phone: 800-518-4726
Email: support@grants.gov
Hours: 24 hours a day, 7 days a week; closed on Federal holidays

eRA Commons Help Desk (Questions regarding eRA Commons registration, tracking application status, post submission issues, FFR submission)

Phone: 301-402-7469 or 866-504-9552 (Toll Free)
TTY: 301-451-5939
Email: commons@od.nih.gov
Hours: Monday - Friday, 7am - 8pm U.S. Eastern Time

CDC Technical Information Management Section (TIMS)
Telephone 770-488-2700
Email: ogstims@cdc.gov
Hours: Monday - Friday, 7am – 4:30pm U.S. Eastern Standard Time

Scientific/Research Contact(s)

Daniel Holcomb
Scientific Program Official
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention (CDC)
Telephone: 770-488-1556
Email: dwh6@cdc.gov

Peer Review Contact(s)

Mikel Walters, PhD

Scientific Review Officer
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention (CDC)
4770 Buford Hwy, NE, Mailstop F-63
Atlanta, GA 30341
Telephone: 404-639-0913 Email: mwalters@cdc.gov

Financial/Grants Management Contact(s)

Manal Ali
Grants Management Specialist
Office of Grants Services
Telephone: 770-488-2706
Email: MAli@cdc.gov

Section VIII. Other Information

Other CDC Notices of Funding Opportunities can be found at www.grants.gov.
All awards are subject to the terms and conditions, cost principles, and other considerations described in the HHS Grants Policy Statement.

Authority and Regulations
Awards are made under the authorization of Sections of the Public Health Service Act as amended and under the Code Federal Regulations.

Awards are made under the authorization of Sections of the Public Health Service Act as

amended and other authority as cited in this NOFO and under the Code Federal Regulations.

All applications submitted for this NOFO must be responsive to the specific requirements and objectives of this NOFO.

Application documents included in an application to a previous NOFO may be submitted as part of this application process. Please read the current NOFO carefully to make sure that what is submitted is consistent with the intent of this NOFO, and that there is an overall match between the proposed research objectives as described in the applicant's abstract and the research objectives of this NOFO.

All applicants are advised to carefully review the responsiveness requirements and instructions on how applicants must document responsiveness in Section III. Part 5 of this NOFO.

Successful grantees may be permitted expanded authorities in the administration of this award as provided for in the Code of Federal Regulations, Title 2, Subtitle A, Chapter II, Part 200, Subpart D, §200.308(d)(4). Specific authorities granted will be detailed in the official Notice of Award document.

RFA-TS-19-002; Amendment 1

CORRECTED Section V. Application Review Information

Corrected scored review criteria categories initially listed in Section V. Application Review Information 1.Criteria

This section corrects and supersedes the categorization of scored review criteria in Section V. Application Review Information 1.Criteria

Significance

- Does the project address an important problem or a critical barrier to progress in the field?
- If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved?
- How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?
- Does the applicant demonstrate an understanding of the source(s) of the PFAS contamination of drinking water?

Investigator(s)

- Are the PD/PIs, collaborators, and other researchers well suited to the project?
- Have they demonstrated an ongoing record of accomplishments that have advanced their field(s)?
- If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?
- Does the application include adequate information on the project team's experience in

conducting research consistent with that proposed in the application's research plan?

Innovation

- Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions?
- Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense?
- Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?
- Is the investigator-initiated proposed research in addition to the core activities innovative and yet offer a reasonable potential of meeting the Purpose and Research Objectives of this NOFO?

Approach

- Do the application's analytic plans effectively describe the research design and hypotheses, data collection measures, and methods to evaluate whether the proposed research plan can effectively address the proposed hypotheses?
- Are the outcomes to be evaluated clearly specified?
- Are the overall strategy, methodology and analyses well-reasoned and appropriate to accomplish the specific aims of the project?
- Are the potential problems, alternative strategies, and benchmarks for success presented?
- If the project is in the early stages of development, will the strategy established feasibility and will particularly risky aspects to be managed?
- If the project involves clinical research are there plans for:
    - Protection of human subjects from research risk
    - Inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?
- Does the applicant propose using a rigorous experimental design that includes data analytic plans appropriate to the research design and hypotheses?
- Are these data appropriate for the research?
- Does the applicant propose a study with adequate sample size to test the proposed hypotheses?
- Do the proposed data collection methods adequately represent the anticipated general core activities for data collection listed in the NOFO?
- Does the applicant provide information on the data sources and methods that will be used in historically reconstruction the PFAS concentration of the drinking water?
- If the site is served by a public water system, does the applicant provide information on the characteristics of the system?
- If the site is served by private wells, does the applicant provide information on the extent of the contamination (e.g. delineation of the groundwater contaminant plume, number of the wells affected?

- Does the applicant address the research objectives as stated in Section I of the NOFO?
- Does the proposed study protocol contain all the necessary elements mentioned in the sample ATSDR protocol (current draft available at https://www.atsdr.cdc.gov/PFAS/PFAS-Research-NOFO.html) ?

Environment:

- Will the scientific environment in which the work will be done contribute to the probability of success?
- Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed?
- Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?
- Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements?
- Are the partnerships necessary and critical for the successful completion of the proposed project documented in the application by letters of support or memoranda of understanding that include detailed information about the nature of existing relationships?
- Does the application demonstrate the organization capacity elements listed in the NOFO?
- Does the applicant organization clearly demonstrate that it will conduct a substantial portion of the research plan, including a proposed budget that does not reflect an intent to act as a "pass through" organization for partner entities?
- Do the submitted letter of support or memoranda of understanding clearly describe the working relationships between the research institution and all partner organizations?
- Is the nature of and the extent of each entity's involvement sufficient for the successful completion of the proposed research project as a whole?
- Does the applicant demonstrate the ability to access the necessary data to execute the research plan?

Added Area of Joint Responsibility in Section VI (4)

- Developing, conducting, and participating in a two-day community engagement PFAS summit in February, 2020 (tentative date) in Atlanta, GA. ATSDR will provide funding for travel, lodging, per diem, and transportation costs for this trip separate from the successful awardees' budgets. Each PI would be responsible for making their travel arrangements to attend this summit.

RFA-TS-19-002; Amendment 1

Multi-Site Study of the Health Implications of Exposure to PFAS-Contaminated Drinking Water

May 9, 2019

Questions and Answers from the Pre-Application Conference Call held on April 29, 2019

Please note that the questions and answers below do not represent an actual transcript of the Pre-Application Call. The information below has been edited to provide the best accuracy, brevity and clarity.

Q1: Page 15 of the RFA (NOFO) states that successful Awardees will be responsible for properly shipping all samples submitted for analysis to the ATSDR-designated laboratory. Will ATSDR or the ATSDR-designated laboratory provide bio-specimen (shipping) supplies and shipping labels to selected sites?

A1: Yes. ATSDR or their designated laboratory will provide biospecimen supplies and shipping labels.

Q2: On page 3 of the RFA, ATSDR outlines sample transfer protocol clarifications for the core protocol.
If additional blood samples are obtained for the express purpose of investigator-initiated research questions involving biomarkers, would the investigator directly receive those samples?

A2: Yes. The investigator would retain (receive) those samples.

Q3: When various publicly available and proprietary data are obtained or purchased for the investigator-initiated research question, it will not be part of the core protocol or core data collection. For these investigator-initiated research projects, can purchased data go directly to the investigator responsible for developing the research question and completing the analyses?

A3: Yes. For investigator-initiated research projects, these data (obtained or purchased by the investigator) would go directly to the investigator.

Q4: A former employee and veteran stated that no veterans are included in any (PFAS) testing and asked why this is so. The caller stated he had been exposed initially in 1973, and the facility closed in 2007.

A4: The ATSDR SME stated that this study (TS19-002) is focused on those individuals who had been exposed recently, no longer than 15 years ago.

Q5: The same caller in Q4 asked where he could go to voice his concerns regarding the health effects of this past exposure.

A5: The results of this study, as well as all the research done on PFAS will be relevant to veterans, as well as anyone else, who was exposed to PFAS. A person does not need to be part of a study for the study's results to be relevant to their situation. It's up to the investigators who prepare applications to choose their sites and study populations.

Q6: We think we may have been exposed, but no one has tested us or our water for PFAS contamination. How will we know whether we qualify for this study?

A6: The inclusion criteria for the study is listed in the NOFO. It will be up to the researchers who propose projects under this study to select the locations and populations for inclusion based on these criteria. These researchers can access ATSDR and other federal government information in order to help with site selection. If your area has not been tested, you may be able to contact your local health or environmental agency to see if

any testing data is available from them. ATSDR has a petition group that an individual or a community group can contact to request an investigation of possible exposure pathways in your community, help community members to learn about a chemical, understand how it could get into their bodies, and help decide how to protect their families and themselves. (For more information on ATSDR petitions please see https://www.atsdr.cdc.gov/hac/petitionatsdrdchi.html **)**

Q7: In several places the RFA (NOFO) states that communities to be studied must be using PFAS-contaminated private wells or community water systems. What levels of PFAS contamination qualify as "current contamination" for these affected systems?

A7: ATSDR is not making any designation or restrictions on the levels of contamination. Researchers need to document what the PFAS level(s) is or has been, in the selected study area and, if the drinking water is no longer contaminated, when the contamination ended. The exposure period is limited to the last 15 years prior to the start of the study. The start of the study will be when the successfully funded awardees actually start their investigations, specifically - recruitment of study participants.

Q8: When we collect biological samples as part of our study, can we freeze the samples for shipment in batches as opposed to shipping every day?

A8: Yes. The samples can be frozen and shipped weekly or at another appropriate rate.

Q9: Will the questionnaire be available only in English? When does ATSDR expect it would it be available in Spanish?

A9: Presently, the questionnaire is available only in English. Depending on the needs of the successful awardees, ATSDR will provide translations of the questionnaire in appropriate languages.

Q10: Which guidance document should we follow, the short RFA document or the longer protocol document?

A10: The core protocol document, accessed by the web link in the NOFO, takes precedence over any other guidance in the NOFO. Applicants and eventual successful grantees will need to follow the ATSDR core protocol.

Q11: In the primary outcomes section of the NOFO, measuring PFAS exposure effects on sex hormones and sexual maturation, vaccine response and neurobehavioral outcomes in children, is mentioned. Is this part of the core protocol?

A11: Yes, measuring exposure effects on sex hormones, sexual maturation, vaccine response and neurobehavioral outcomes in children are part of the current core protocol.

Q12: Is it possible to split samples for laboratory analysis for the investigator initiated investigation or do entire samples need to go to ATSDR, and then be requested back for use by the investigator?

A12: Split samples will be permitted.

Q13: The question of whether this study will explore cancer endpoints has been in the press. Is a relationship between PFAs exposure and cancer a reasonable subject for proposed investigator initiated research under this NOFO?

A13: You'll need to have the appropriate sample population size. The sample population size specified by ATSDR for this investigation would not be of sufficient statistical power to effectively evaluate kidney or testicular cancer effects. ATSDR may look at cancer occurrences in the study population based on questionnaire responses and associated medical records, but we do not expect to have enough statistical power during this study to effectively evaluate cancers based on these data. You may propose cancer outcomes as part of an investigator initiated study, but please remember to make the best case for your expected research proposals in your application. Even though the goal of this study is not primarily cancer-related, you may propose cancer biomarkers or intermediary cancer endpoints with the limitations discussed above.

Q14: A number of health association studies are planned as part of the ATSDR core protocol. Some will require pooling the data across all the sites involved in this study, others may not. Will investigators make the determination which of these will be done in parallel and which will wait for pooled data?

A14: ATSDR intends that the analysis of those endpoints as part of the core protocol will be based on pooled data. However, investigators are free to analyze the data they collect as well as propose additional data analyses as part of an investigator initiated study.

Q15: Will health association for the core analyses be done by ATSDR or a team across sites or should we include this as part of our proposals at each site?

A15: Both ways. The data will be aggregated and there will be coordination among the sites and ATSDR. We do plan to involve successful awardees in the statistical analysis of the aggregated data. We also expect that there will be some type of publication committee including ATSDR and the study sites that will decide which health outcomes or which plans of analysis to coordinate across all the selected sites. Since this is a cooperative agreement, we anticipate that there will be extensive coordination and collaboration between the successful awardees and ATSDR staff during this study regarding these and other decisions.

Q16: Will CNS (testing) joint training across sites be given in order to get more uniform data?

A16: Yes, that's a possibility, depending on the logistics involved after the successful awardees are selected. The core neurobehavioral testing requirements include certain qualifications for those individuals who will be administering these tests at each selected site. It's up to the applicant to ensure that they include personnel in their plans who meet these various levels of qualifications.

Q17: There's a great deal of specificity I the protocol for sampling but not so much for dose reconstruction. Are you looking at this as an investigator initiated approach and do you have some level of specificity that you're looking for?

A17: There are various approaches for dose reconstruction and it depends on the site(s) selected. For example, some sites may require groundwater contaminant fate and transport modeling. We expect applicants to know about the exposure scenario situation at their proposed sites and have some expertise in modeling the movement of the contaminants to the drinking water source, and in drinking water system distribution modeling, as appropriate. ATSDR staff will be able to share their experience and expertise

with successful awardees in these areas.

Q18: The RFA states that the site can be an industrial facility or an AFFF site. Is there a preference?

A18: No.

Q19: Can you confirm that each site will conduct their own site-specific analyses and write papers about the analyses from their own site?

A19: Yes, that's true.

Q20: Will all require manuscripts resulting from the project be subject to CDC clearance or only those which include CDC staff as authors?

A20: All resulting manuscripts will be subject to CDC clearance, since they are sponsored by CDC/ATSDR.

Q21: Does the investigator initiated research need OMB approval?

A21: No. IRB approval may be needed, though, depending on what is proposed.

Q22: How do you plan to manage year two (of the study) when all your grantees have their highest costs?

A22: Applicants should include in their applications a proposed budget for each year of the five-year expected period of performance, based on their expectations of activities and associated costs. There is a process for carrying over unspent grant funds into a following year, as long as a reasonable justification for appropriate use of funds is submitted with the carryover request. The ceiling and floor funding amounts in this NOFO were designed for maximum flexibility of projects submitted in response to this NOFO.

Q23: There are separate gift cards (proposed in the protocol) for (study participants who) complete the questionnaire and who provide a biological sample. Does that mean that a person who participates in the study can be included in the analysis if they provide one or the other?

A23: We want successful awardees to collect both a questionnaire and biological samples from study participants.

Q24: The expected timeline in the NOFO notes that the final protocol will be reviewed and approved by month 18, and all the samples will be collected by month 24. This leaves six to twelve months to perform the data collection. Given that some samples must be "fasting" samples, is it possible to allow participants to complete the questionnaire at a separate time or by telephone?

A24: It's up to the applicants to propose their preferred data collection methods and justify their plans. A concern is that study participants may not choose to provide both answers to a questionnaire and a biological sample if these are done at different times.

Q25: In terms of eligibility for our recruitment, are we able to take volunteers or do we need a completely random sample population, as long as they meet all of the requirements for participation.

A25: Yes. An applicant can decide to include volunteers.

Q26: What is your experience or expectation regarding the amount of time that will be needed

for Office of Management and Budget (OMB) clearance?

A26: We've already initiated the clearance process and have submitted the clearance "package" for the core protocol required to publish the mandatory 60 day notice for public comment. We anticipate six to nine months to receive OMB approval. This will depend on any additional information OMB may require beyond the initial submission, but at this time we expect that the schedule contained in the NOFO will be fairly accurate. The initial OMB approval will be for three years, and an extension may be filed as well.

Q27: Is there a possibility of extending the data collection window depending on when OMB clearance is received?

A27: Yes. The timelines can be adjusted as the study proceeds.

Q28: Will participants' cancer results from this study be included in the cancer5 registry?

A28: We assume so.

Q29: Can applicants' proposed budgets include a major equipment purchase such as a freezer for sample storage?

A29: Yes.

Q30: Is it better for applicants to propose studying one community or multiple communities?

A30: Either is fine. Please include the best justification for your plans in your application.

Q31: Is there a limit or percentage on how much money that can go out to the studied communities?

A31: It's up to the applicant to propose how the awarded funds are distributed.

Q32: Is the funding ceiling expected to be constant across all the years in the period of performance?

A32: We can only guarantee the first year of funding, as our funding is allocated on a yearly basis. However, we are currently planning on providing this level of funding for each year in the period of performance.

Q33: Do we have the ability to modify or add components to the RedCap application?

A33: You may add components but must keep the core activity questionnaire component.

Q34: Will ATSDR provide a programmed REDCap database or will applicants be expected to program it from the provided questionnaires?

A34: It will be programmed by ATSDR or ATSDR's designated contractor.

Q35: Can you give us guidance on page limits for our applications?

A35: Page limits are listed in the NOFO. For this specific NOFO, the Research Strategy component of the Research Plan narrative is limited to 20 pages. Supporting materials for the Research Plan narrative included as appendices may not exceed 10 PDF files with a maximum of 50 pages for all appendices. Do not use the appendix to circumvent page limits. A maximum of 10 PDF documents are allowed in the appendix. Additionally, up to 3 publications may be included that are not publically available. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

Q36: The NOFO mentions both pharmacokinetic modeling and physiologically-based pharmacokinetic modeling. Is physiologically-based pharmacokinetic modeling a requirement?

A36: No, it's not a requirement. Applicants could propose, for example, a single-compartment model (i.e., a pharmacokinetic model). Be sure and provide a justification in your application for your proposed modeling based on which PFAS compound(s) you are studying.

Q37: If physiologically-based pharmacokinetic modeling is being used across the consortium of investigators, would expect that a standardized model will be used?

A37: This would need to be worked out among the successful awardees and ATSDR staff during the course of the study. Ultimately, we want to have some method of estimating PFAS serum levels based on drinking water concentrations.

Q38: Is a pregnancy cohort considered responsive to this RFA?

A38: Yes, as long as they meet the age ranges and other criteria listed in the NOFO.

Q39: Can one extend the survey questions beyond those listed in the core protocol to address confounders?

A39: Sure. These may prove useful to other successful applicants as well.

Q40: What percent pass-through is allowed in the budget?

A40: There is no stated percentage, but this would need to be reviewed to determine whether the pass-through is reasonable and allowable. However, a substantial portion of the proposed research work plan must be carried out by the applicant organization throughout the project period and the applicant organization cannot serve as a "pass through" to fund another entity to conduct the majority of the research. It's up to the applicant to make the best case for funding, how and where they plan to conduct the research, and who is going to perform the research activities in partnership with ATSDR.

Q41: Should the Data Management Plan be part of the Appendix in our applications?

A41: Applicants that plan to collect public health data must submit a Data Management Plan (DMP) in the Resource Sharing Plan section of the PHS 398 Research Plan Component of the application. If you need to put it in your Appendix due to page limitations, please be sure to include a reference to its location in the Research Strategy section of your application.

Q42: What type of PDF documents are allowed in the Appendix of our application? Could an unpublished manuscript be included in the Appendix?

A42: Supporting materials for the Research Plan narrative included as appendices may not exceed 10 PDF files with a maximum of 50 pages for all appendices. Do not use the appendix to circumvent page limits. A maximum of 10 PDF documents are allowed in the appendix. Additionally, up to 3 publications may be included that are not publically available. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide. An unpublished manuscript could be included, subject to the limitations mentioned.

Q43: The protocol lists a specific volume of blood that needs to be drawn. Could we increase

that amount in order to provide split samples and test for additional biomarkers?

A43: The amount of blood sample specified in the core protocol is what we anticipate is needed for the core activities. It's up to the applicant to justify any additional amount.

Q44: Is the exposure in the study population required to be above the EPA 70 parts per trillion health advisory level?

A44: No.

Q45: Could we propose including a lower but exposed reference population in our study?

A45: That would be fine.

Q46: Is there a targeted enrollment for each site?

A46: There is not. We want a total enrollment over all the funded sites of at least 6,000 adults and 2,000 children. It's up to the applicant to justify their proposed sample (population) size based on the exposure scenario. Please keep in mind that a smaller sample size would justify a lower budget amount for your proposed activities.

Q47: Do applicants need to propose enrolling both adults and children, or is "either or" OK?

A47: ATSDR would prefer applicants propose enrolling both adults and children in their applications.

Q48: Willow Grove and the Warminster areas have already been tested by ATSDR. Based on that, are there any further studies planned or are you going to concentrate on the other eight areas?

A48: You're referencing ATSDR Exposure Assessments. Those assessments are separate from this study.

Q49: If a site was subject to an exposure assessment, would that data be available for inclusion in this study?

A49: Those assessments are separate from this study. However, those assessment sites are not necessarily excluded from being proposed for this study. Any site that meets the criteria listed in the NOFO can be proposed as a study site under this NOFO. If a site was subject to an exposure assessment, or if PFAS biomonitoring had previously been conducted at a site, the applicant can use these data in estimating historical PFAS serum levels. However, for the study covered by this NOFO, new serum samples must be obtained from participants for the analyses of PFAS levels and the effect biomarkers.

Q50: Is it possible with the appropriate forms and consent to aggregate the data from the exposure assessment sites?

A50: Health data is not included in the exposure assessments, so there is no data to aggregate.

Q51: Is there an implicit implication that the study population should have been exposed to PFOS and/or PFOA?

A51: No.

Q52: Would it be possible to explore the possibility of selecting participants from ATSDR

exposure assessment sites and conducting clinical sampling with them?

A52: Again, it's not a requirement that proposed sites for this study have had an ATSDR Exposure Assessment done. Those assessments are separate from this study. It is possible to select participants from ATSDR exposure assessment sites, but new blood samples must be taken so that analyses of PFAS levels and effect biomarkers can be conducted.

Q53: In the NOFO's purpose, what biomarkers do you expect could be derived from pharmacokinetic modeling?

A53: None. We are talking about exposure and estimating historic PFAS serum levels and comparing those to health outcomes.

Q54: Given the speed of new information coming out regarding PFAS, how flexible is the OMB "package" to changes in order to include new or additional survey questions?

A54: It is possible to modify questionnaires. There is a process for that. However, applicants are cautioned to avoid being too creative with modifications to approved forms because OMB may determine that modifications substantially change the original proposal and require us to restart the approval process. Any modifications the successful grantee group would like to do for the core protocol should be discussed among the ATSDR and grantee Principal Investigators (PIs) to decide whether the change warrants the process of submitting a change request and hoping that OMB does not determine it is a substantial change. Another possibility is to add or propose additional questions as part of an applicant's investigator initiated protocol. Investigator initiated protocols would not need OMB approval.

Q55: Are we going to provide honoraria for those involved in the study's community boards?

A55: Applicants can include these in their proposed budgets. The amounts would be subject to review and approval by CDC Office of Grant Services on an individual basis to make sure they are allowable and appropriate.

Q56: In terms of the review criteria, how will you weight how well each applicant helps ATSDR meet their research goals for this study vs. the novelty of the investigator initiated studies?

A56: The core activities are essential in your proposal. Each proposal is scored individually, not compared to any other. The peer reviewers will be instructed to follow the critique template and consider all the criteria listed in the NOFO.

Q57: In terms of the review criteria, should the investigator initiated studies proposed be health-based or based more on environmental sampling?

A57: It's up to the applicant to choose the focus of the investigator initiated studies proposed.

Q58: Is the data report considered to be operated on behalf of the agency so that it will be NIST 800-53 or is it considered to be handled by an internal contractor so it will be NIST 800-171?

A58: All data resulting from the sample analysis will be stored directly by ATSDR. ATSDR will share each site's sample testing results with them in addition to additional de-identified data for all sites. ATSDR will provide a REDCap secure web application for building and managing online surveys and databases (at no cost to the awardee) that

includes all ATSDR data requirements such as variable names, data types (numerical, text, drop-down list, etc.), controlled vocabulary, value range, and so on. The REDCap application provided by ATSDR will also contain a database for data storage, data entry forms for various study surveys/questionnaires, and data validation rules. ATSDR will consolidate and integrate all data from successful grantees to support epidemiological and statistical analyses, including those above at a larger scale (i.e., across multiple sites). Applicants that plan to collect public health data must submit a Data Management Plan (DMP) in the Resource Sharing Plan section of the PHS 398 Research Plan Component of the application. Applicants are responsible for the security of the databases they operate and maintain.

Q59: Can you confirm that the proposed investigator initiated research should be woven into one big proposal vs. two separate proposals?

A59: Yes. One coordinated proposal would be best.

Q60: When will the amended NOFO be published?

A60: As soon as possible before the due date for applications.

Q61: Can you give us more information regarding the medical record extraction process?

A61: There is a form in the protocol. We want to get enough information to confirm a participant's response. The applicant would abstract and keep any medical records received and provide ATSDR with the results/confirmation.

Q62: Will you be doing any historical exposure reconstruction based on the ATSDR Health Assessments?

A62: No and also not for this study. Those assessments are separate from this study.

Q63: The NOFO mentions the possibility of additional funding becoming available for this study. Is it possible that additional funds will be available in Year one for this study?

A63: The NOFO mentions additional funding may become available during the entire period of performance. Only the funding listed for the first year of the study should be considered at this time.

Q64: There is a wide range of ages listed for children's eligibility for inclusion in this study. Is it ATSDR's expectation that applicants will recruit participants from the entire age range or select a narrower age range?

A64: It's up to each applicant to propose and justify in their application their chosen recruiting criteria within the stated range.