Billing Code: 4163-18-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Toxic Substances and Disease Registry

[30Day-20-19ACF]

Agency Forms Undergoing Paperwork Reduction Act Review

In accordance with the Paperwork Reduction Act of 1995, the Agency for Toxic Substances and Disease Registry (ATSDR) has submitted the information collection request titled "Human Health Effects of Drinking Water Exposures to Per- and Polyfluoroalkyl Substances (PFAS): A Multi-site Cross-sectional Study (The Multi-site Study)" to the Office of Management and Budget (OMB) for review and approval. ATSDR previously published a "Proposed Data Collection Submitted for Public Comment and Recommendations" notice on April 23, 2019 to obtain comments from the public and affected agencies. ATSDR received two comments related to the previous notice. This notice serves to allow an additional 30 days for public and affected agency comments.

ATSDR will accept all comments for this proposed information collection project. The Office of Management and Budget is particularly interested in comments that:

(a) Evaluate whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information will have practical utility;

(b) Evaluate the accuracy of the agencies estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used;

(c) Enhance the quality, utility, and clarity of the information to be collected;

(d) Minimize the burden of the collection of information on those who are to respond, including, through the use of appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology, e.g., permitting electronic submission of responses; and

(e) Assess information collection costs.

To request additional information on the proposed project or to obtain a copy of the information collection plan and instruments, call (404) 639-7570 or send an email to omb@cdc.gov. Direct written comments and/or suggestions regarding the items contained in this notice to the Attention: CDC Desk Officer, Office of Management and Budget, 725 17th

Street, NW, Washington, DC 20503 or by fax to (202) 395-5806. Provide written comments within 30 days of notice publication.

Proposed Project

Human Health Effects of Drinking Water Exposures to Per- and Polyfluoroalkyl Substances (PFAS): A Multi-site Cross-sectional Study (The Multi-site Study)– NEW – Agency for Toxic Substances and Disease Registry (ATSDR).

Background and Brief Description

Per- and polyfluoroalkyl substances (PFAS) are a family of chemicals used in industrial applications and consumer products. PFAS contamination of drinking water is widespread in the U.S. Some estimates indicate that at least sixty million residents were served by 66 public water supplies that had at least one sample at or above the US Environmental Protection Agency (EPA) Lifetime Health Advisory for perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) (individually or combined), which is 70 nanograms per liter (ng/L) of water. Industrial facilities that manufacture or use PFAS have contaminated drinking water in surrounding communities in several states. In addition, PFOS, PFOA, perfluorohexane sulfonic acid (PFHxS) and other PFAS chemicals are constituents in aqueous film-forming foam (AFFF), used to extinguish flammable liquid fires. The use

of AFFF at military bases and other sites may have resulted in the migration of PFAS chemicals through soils to ground water and/or surface water sources of drinking water for the bases and/or surrounding communities around the country.

In response to growing awareness of the extent of PFAS contamination across the U.S., the Section 316(a) of the 2018 National Defense Authorization Act (P.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), authorized and appropriated funds for the Agency for Toxic Substances and Disease Registry (ATSDR) to conduct a study on the human health effects of PFAS contamination in drinking water. The existence of widespread contamination at many sites across the U.S. makes this a paramount effort in addressing the health effects of exposures to PFAS from contaminated drinking water. Consequently, ATSDR is requesting a three-year Paperwork Reduction Act (PRA) clearance for the Multi-site Study.

The Multi-site Study builds on activities undertaken in preparing and conducting the data collection for the proof-of-concept study at the Pease International Tradeport in Portsmouth, New Hampshire (the Pease Study) (OMB Control No. 0923-0061; expiration date 08/31/2022). These activities included developing data management systems and community engagement materials, modifying the childhood neurobehavioral

test battery, adjusting blood collection volume, and modifying data collection materials such as the childhood questionnaire and medical records abstraction forms. Based on peer reviewer and OMB comments on the Pease Study, the Multi-site Study protocol now includes additional data analyses to address potential biases such as selection bias and confounding.

ATSDR will conduct this research using a cooperative agreement titled "Multi-site Study of the Health Implications of Exposure to PFAS-Contaminated Drinking Water" (Notice of Funding Opportunity [NOFO] No. CDC-RFA-TS-19-002). Seven research recipients have been selected: University of Colorado School of Public Health, Michigan State Department of Health and Human Services, Pennsylvania Department of Health and RTI International, Rutgers School of Public Health, Silent Spring Institute, SUNY at Albany and the New York State Department of Health, and the University of California at Irvine.

The Multi-site Study is designed to aggregate data across all recipient sites and is designed to compare data between sites. The main goal of this cross-sectional study is to evaluate associations between measured and reconstructed historic serum levels of PFAS including PFOA, PFOS, and PFHxS, and selected health outcomes. The health outcomes of interest include lipids, 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. In addition, the study will investigate PFAS differences in sex hormones and sexual maturation, vaccine response, and neurobehavioral outcomes in children. In adults, additional outcomes of interest include cardiovascular disease, osteoarthritis and osteoporosis, endometriosis, and autoimmune disease.

Under the cooperative agreement, each recipient proposed candidate study sites at communities whose drinking water was impacted by AFFF use or by industrial PFAS releases. Site selection considered the documented levels of PFAS drinking water concentrations. The aim was to include sites so that a wide range in PFAS exposures levels were included in the study. This will enable the evaluation of exposure-response trends including effects at the lower range of exposures. Ground water contaminant fate and transport models and water distribution system models may be necessary to identify the areas with contaminated drinking water, to determine the period when the drinking water was contaminated, and to reconstruct historical PFAS contaminant concentrations.

For exposure estimation, participants will be categorized based on their measured serum concentration of PFAS compounds or on modeled estimated historical serum levels (e.g., referent or low, medium, high). Measured and estimated PFAS serum levels

will also be evaluated as continuous variables. At sites with prior PFAS biomonitoring data, the study will evaluate changes in PFAS concentration over time.

Each recipient shall reconstruct historic serum PFAS concentrations. This may be done by estimating half-lives and elimination rates as well as by water contamination modeling to inform pharmacokinetic (PK) or physiologically based pharmacokinetic (PBPK) models. Historical serum PFAS reconstruction will enable the evaluation of exposure lags and vulnerable periods as well as statistical analyses that can control for confounding and reverse causation due to physiological factors.

If feasible, each recipient shall identify and enumerate all households served by the contaminated drinking water supply in the selected community to recruit potential participants and to meet the sample size requirements for children and adults. If the selected community is served by a PFAS-contaminated public water system, then the recipient will obtain a list of households served by the water purveyor from its billing records. If the community is served by contaminated private wells, then the recipient will obtain a list of households with contaminated wells from the local and/or state health and environmental agencies.

Statistical sampling methods (e.g., a two-stage cluster sample) may be used for recruitment of study participants if all the affected households can be enumerated. If the PFAS drinking water concentrations vary widely across the community, then the recipient should consider using targeted sampling approaches - including oversampling of areas with higher PFAS concentrations - to ensure a sufficiently wide distribution of exposure levels among study participants to evaluate exposure-response trends. If enumeration of all households is not feasible, or if participation rates are expected to be low, then the recipient can consider non-probabilistic sampling approaches such as "judgment" and "snowball" sampling approaches.

The recipients should consider requesting assistance from local and state health departments in their recruitment efforts. In addition, the recipients should engage community organizations to assist in conducting outreach about the study and recruitment of participants and consider establishing a community assistance panel (CAP). The CAP could provide comments on any additional investigator-initiated research questions and hypotheses and facilitate the involvement of the affected community in decisions related to outreach about the study, participant recruitment strategies, and study logistics. The CAP could also assist the recipient in the dissemination of study findings to the community.

In total, ATSDR seeks to enroll approximately 9,100 participants (7,000 adults and 2,100 children and their parents) from communities exposed to PFAS-contaminated drinking water over the first three years of the five-year cooperative agreement program. In total, each recipient will attempt to meet a target recruitment of 1,000 adults and 300 children. Annualized estimates are 3,033 participants (2,333 adults and 700 children).

To restrict this study to drinking water exposures, adults occupationally exposed to PFAS will not be eligible for the study (e.g., ever firefighters or ever workers in an industry using PFAS chemicals in its manufacturing process). Likewise, children whose birth mothers were occupationally exposed will not be eligible.

Assuming a 95 percent eligibility rate and a 40 percent response rate, ATSDR estimates that the recipients will screen 7,982 people (6,140 adults and 1,842 children) each year across all sites in order to recruit the target sample size of 3,033 participants (2,333 adults and 700 children), using an annual time burden of 1,330 hours. The recipients will provide appointment reminder calls for each eligible person who agrees to be enrolled (n=3,033 per year).

At enrollment, each recipient will obtain adult consent, parental permission, and child assent before data collection

begins. For each participant, the recipient will take body measures, collect blood samples to measure PFAS serum levels and several effect biomarkers such as lipids, and thyroid, kidney, immune and liver function. The recipient will also obtain urine samples from participants to measure PFAS levels and kidney function biomarkers. The study will archive leftover serum and urine samples for additional analyses of PFAS chemicals and specific effect biomarkers. The National Center for Environmental Health (NCEH) laboratory will perform blood and urine PFAS analyses for all Multi-site Study participants. Thus, issues of inter-laboratory variability for exposure measures will be eliminated.

Adult participants and a parent of child participants will complete a questionnaire that includes residential history, medical history, occupational history, and water consumption habits (n=3,033 adults and 700 children per year). Ideally, the parent will be the child's birth mother, as ATSDR will ask details about the child's exposure, pregnancy, and breastfeeding history. For purposes of time burden estimation, ATSDR assumes that 20 percent of parents (n=140 per year) will also enroll as adults and can take the child short form questionnaire; therefore, 560 parents will take the child long form questionnaire per year. Parents and children, with administration by trained professionals, will also complete

neurobehavioral assessments of the child's attention and behaviors (n=700 per year). The time burden for responding to questionnaires is 1,482 hours, and for neurobehavioral assessments is 1,225, per year.

To facilitate access to medical and school records, each recipient will reach out to local medical societies, public school systems, and private schools, to enlist their cooperation with the study. The recipient will ask for permission to abstract participants' medical records to confirm self-reported health outcomes. The recipient will also seek permission to abstract and compare children's school records to their behavioral assessment results. Based on ATSDR's experience from the Pease Study (OMB Control No. 0923-0061; expiration date 08/31/2022), ATSDR estimates that it will take 30 school administrators, 48 education specialists, 70 medical office administrators, and 150 adult and 50 pediatric medical record specialists to complete record abstractions across all study sites. The annual time burden for medical and educational record abstraction is estimated to be 2,490 hours.

The total annualized time burden requested is 7,960 hours. There is no cost to the respondents other than their time.

Estimated Annualized Burden Hours

Type of	Form Name	Number of	Number of	Average

Respondents		Respondents	Responses per Respondent	Burden per Response (in hours)
Multi-site Study Participants	Eligibility Screening Script	7,982	1	10/60
	Appointment Reminder Telephone Script	3,033	1	5/60
	Update Contact Information Hardcopy Form	3,033	1	5/60
	Medication List	3,033	1	3/60
	Body and Blood Pressure Measures Form	3,033	1	5/60
	Blood Draw and Urine Collection Form	3,033	1	10/60
	Adult Questionnaire	2,333	1	30/60
	Child Questionnaire – Long Form	560	1	30/60
	Child Questionnaire – Short Form	140	1	15/60
	Parent Neurobehavioral Test Battery	700	1	15/60
	Child Neurobehavioral Test Battery	700	1	90/60
Medical Office	Request for Medical	70	43	20/60

Administrators	Record Abstraction			
Medical Record Specialists	Medical Record Abstraction Form - Adult	150	16	20/60
	Medical Record Abstraction Form - Child	50	14	20/60
School Administrators	Request for Child School Record Abstraction	30	23	20/60
Education Specialists	Child School Record Abstraction Form	48	15	20/60

Jeffrey M. Zirger,
Lead, Information Collection Review Office,
Office of Scientific Integrity,
Office of Science,
Centers for Disease Control and Prevention.

[FR Doc. 2019-27550 Filed: 12/20/2019 8:45 am; Publication Date: 12/23/2019]