Evaluating the Association between Serum Concentrations of Per- and Polyfluoroalkyl Substances (PFAS) and Symptoms and Diagnoses of Selected Acute Viral Illnesses

OMB Control No. 0923-NEW

New Information Collection Request

Supporting Statement Part B –

Collections of Information Employing Statistical Methods

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Date: 07/29/2022

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Part B. Collections of Information Employing Statistical Methods

B.1. Respondent Universe and Sampling Methods

This is a follow-up study aiming to recruit approximately 2,800 and 370 child participants from existing ATSDR PFAS cohorts, specifically individuals for whom CDC/ATSDR already has measured serum-PFAS concentrations. CDC/ATSDR will only recruit participants who gave written informed consent to be contacted for additional studies in the future, and who consented for their PFAS serum data to be used in future studies. CDC/ATSDR will invite participants to complete a new series of surveys to determine whether PFAS exposure increases susceptibility to viral infections, including, but not limited to COVID-19.

(Per- or Polyfluoroalkyl Substances Exposure Assessments (PFAS EAs) Cohort
OMB Control No. 0923-0059, expiration date 06/30/2022)

In 2019 and 2020, the Agency for Toxic Substances and Disease Registry (ATSDR) conducted statistically based biomonitoring PFAS exposure assessments (EAs) in eight communities that had documented exposures to PFAS in drinking water. ATSDR also supported two EAs that were designed to test the PFAS Exposure Assessment Technical Tools (PEATT). PFAS concentrations were measured in serum collected from EA and PEATT assessment participants, and a survey was administered to gather information to characterize each individual's exposure. These communities were investigated under "Per- or Polyfluoroalkyl Substances Exposure Assessments [PFAS EAs]" (OMB Control No. 0923-0059, expiration date 06/30/2022).

Based on preliminary review of the informed consent forms obtained, nearly all (approximately 99%) PFAS EA and PEATT participants gave consent for additional contact. The EAs used a one-stage cluster sample, in which each household in the area receiving impacted water was a cluster and all individuals in a selected household were included in the sample. Clusters (households) were randomly selected from the sampling frame. This yielded a representative sample of the population in the area potentially impacted by PFAS contamination of drinking water. Written informed consent (including Privacy Act Statement, consent, assent, and parental permission forms) was obtained from participants upon sample collection; these forms are securely archived at ATSDR. The PEATT assessments were conducted by state health departments using a similar sampling design. A more detailed discussion of the PFAS EA Cohort and PEATT is found in the Protocol.

Human Health Effects of Drinking Water Exposures to Per- and Polyfluoroalkyl Substances (PFAS) at Pease International Tradeport, Portsmouth, NH (The Pease Study) Cohort
OMB Control No. 0923-0061, expiration date 08/31/2022

The cross-sectional Pease Study aims to enroll a convenience sample of participants who were eligible for the 2015-2017 Pease biomonitoring program (Daly et al., 2018; DHHS, 2016) and a small number of referents from other areas of New Hampshire. The Pease Study aims to recruit

1,100 adults and 525 children. Written informed consent (including Privacy Act Statement, consent, assent, and parental permission forms) are obtained from participants; these forms are being securely archived at ATSDR. Recruitment for the Pease Study was completed on December 31, 2021, with 781 adults and 178 children enrolled in the study. A more detailed discussion of the Pease Study Cohort is found in the Protocol.

Statistical Power Calculation

All eligible participants enrolled in these CDC/ATSDR cohorts will be asked to participate in this follow-up study. Our goal is to recruit a total of 2,800 adults and 370 children. Power calculations based on the estimated sample size from these cohorts can be found in the Protocol. These power calculations, assuming a universe of eligible participants of 3,200, were calculated using a range of response rates, hazard ratios, event probabilities, and degrees of correlation between prediction variables.

Sampling Plan

This study will invite the entire universe of eligible participants to participate (i.e., all participants already enrolled in CDC/ATSDR cohorts, who meet the eligibility criteria described above). We anticipate that the total number of participants enrolled in the CDC/ATSDR cohorts will be around 3,170 individuals. Therefore, our target sample size is 3,170. Recruitment packages will be sent to all participants across the 11 sites at the same time.

B.2. Procedures for the Collection of Information

Details on the procedures for the collection of information are available in the Protocol. They are summarized below.

Participant Recruitment

A recruitment packet will be mailed to all participants included in the PFAS cohorts who agreed to be contacted for follow-up studies. Participants will be asked if they would like to participate in a follow-up study on viral infections, including but not limited to, COVID-19. Mailed recruitment packets will contain a letter of invitation (**Appendix G**), consent forms (two copies, one to keep and one to sign and return) (**Appendix H-I**), and Privacy Act Statement (**Appendix K**). They will also include an initial paper-based survey (**Appendix A, B**), symptom diary (**Appendix E**), recruitment FAQs (**Appendix G2**), and stamped return envelope. Participants recruited from the PEATT study will also receive a cover letter from our state partners (**Appendix G1**). Participants who agree to take part in this new study will be asked to return their signed consent forms and initial paper-based surveys using the provided return envelope.

Data Collection

Completed initial surveys received without a signed consent form will be destroyed. On the consent form, participants will be asked their preferred mode of collection for the follow-up surveys: paper-based (**Appendix C, D**) or web-based (**Appendix C1, D1**). Web-based surveys will be administered through REDCap, a secure web application for managing surveys.

After the initial paper-based survey is received, participants in this study will be asked to complete a series of four follow-up surveys. Based on their stated preference during informed

consent, every three months, participants will receive either paper-based (**Appendix C, D**) or web-based follow-up surveys (**Appendix C1, D1**), for a total of four follow-up surveys.

The initial and follow up surveys will be timed to collect information throughout a whole year, including an entire flu season. To improve recall of symptoms between surveys, participants will also be asked to keep a symptom diary (**Appendix E**). The participant may use the diary to complete the periodic surveys; this diary will not be returned back to ATSDR.

Data Management

CDC/ATSDR will implement a Data Management Plan for the data collected for this study per ATSDR guidance (STARS).

B.3. Methods to Maximize Response Rates and Deal with Non-response

A recruitment letter (**Appendix G**) will be sent to all participants from CDC/ATSDR cohorts who consented to be contacted for follow-up studies. Prior to sending the recruitment packets, potential participants will be made aware of this upcoming study with a recruitment postcard and fact sheet (**Appendix G2**) Because these participants have already consented to be contacted for follow-up, we anticipate high response rates (estimated response rate of 85%). If potential respondents have not responded to the recruitment letter within four weeks, we will attempt to contact those individuals by phone (**Appendix L**) a maximum of two times for recruitment. The same follow-up procedures will be followed for follow-up surveys as well. Follow-up will be attempted two weeks after REDCap follow-up surveys are sent and four weeks after paper-based follow-up surveys are sent. Additionally, CDC/ATSDR will leverage existing relationships in these communities to promote the studies; these outreach activities will include promoting the study at community meetings and including information in existing community newsletters. CDC/ATSDR is working internally to coordinate these outreach activities with the existing infrastructure in place from the Pease, PEATT, and EAs.

Participants will be offered an incentive to participate in the study, with incentives of $10 provided for each completed survey of up to 5 returned, with an additional $25 when all 5 surveys are returned, up to $75 in total for participants who complete all 5 surveys. Monetary incentives, including those as low as $1, are associated with higher response rates compared with nonmonetary incentives (Cho, Johnson, & Vangeest, 2013).

To improve response rates, we will ask participants how they prefer to complete their follow-up surveys – through paper-based or web-based surveys. Cohort members will indicate their preference when they enroll by consenting to be a part of the study. Additionally, participants who initially select paper-based surveys will be asked on each subsequent paper-based survey if they would like to switch to web-based surveys for the rest of the study. The initial packets (including recruitment materials, consent forms and initial surveys) will all be paper-based and sent by mail, because mailed invitation letters are associated with higher responses rates for

both paper- and web-based surveys (Converse, Wolfe, Huang, & Oswald, 2008; Freedman, McGonagle, & Couper, 2018).

B.4. Test of Procedures or Methods to be Undertaken

CDC/ATSDR pilot tested the surveys for functionality, ease of use and comprehension, and time burden measurement in May 2021 among nine CDC/ATSDR employees.

All outcome definitions are based on previously defined syndrome definitions that have been used in peer-review journal articles or are recommended by national and international agencies. These previous studies collected this information through self-reported surveys as well. These studies have analyzed symptoms individually (Dalsager et al., 2016) as well as for syndrome definitions (Aiello et al., 2012; Eckardt & Baumgart, 2011; Fitzner et al., 2018; Hall et al., 2011; Sandora et al., 2005)

The Protocol describes these syndrome definitions in more detail (Methods Section & **Appendix F**).

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

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