

Human health effects of drinking water exposures to per- and polyfluoroalkyl substances (PFAS): A multi-site cross-sectional study

(The Multi-site Study)

New Information Collection Request

Supporting Statement Part B –

Collections of Information Employing Statistical Methods

Principal Investigator: Marian Pavuk, MD, PhD

Title: Senior Epidemiologist, Environmental Epidemiology Branch

Email: fsh8@cdc.gov

Phone: 770-488-3671

Fax: 770-488-1541

Date: April 24, 2020

Table of Contents

B.1. Respondent Universe and Sampling Methods.....	3
B.2. Procedures for the Collection of Information.....	5
B.3. Methods to Maximize Response Rates and Deal with Non-response.....	6
B.4. Test of Procedures or Methods to be Undertaken.....	8
B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data.....	9
References.....	13
List of Appendices.....	13
Multi-site Study Protocol and Attachments.....	13

Part B. Collections of Information Employing Statistical Methods

B.1. Respondent Universe and Sampling Methods

Statistical methods will be used to recruit participants for the Multi-site Study where applicable. If information is not available to use statistically based methods, non-probabilistic sampling methods (e.g., “snowballing” sampling or respondent-driven sampling), may be used. The respondent universe and the rationale for using statistically based or non-probabilistic sampling methods are described in the **Multi-site Study Protocol**. In general, the recruitment strategies are to be “exposure-driven” in order to achieve a wide distribution of exposure levels among study participants. The main goals of the research study are to examine associations between health outcomes and measured and historically reconstructed serum levels of PFAS.

Respondent Universe: In summary, recipients and ATSDR will enroll approximately 9,100 participants (7,000 adults and 2,100 children and their parents). Each cooperative agreement recipient will attempt to meet a target recruitment of 300 children and 1,000 adults.

The study populations and eligibility are discussed in the **Multi-site Protocol Section 3.2**. Statistical justification for desired sample sizes is provided in **Multi-site Study Protocol Section 3.3** and in more detail in **Attachment 3**.

Adults will be 18 years or older, and children will be 4-17 years of age at enrollment. Ideally, the parent should be the mother, who can best answer some survey questions about the child's exposures and about the mother's pregnancy and breastfeeding history. A parent can enroll with more than one child. In this case, the recipients (ATSDR awardees) will enroll each child separately along with his or her parent. Parents, if eligible, may also enroll in the adult study.

To restrict this study to drinking water exposures, any adult occupationally exposed to PFAS will not be eligible for the study (i.e. ever firefighters or in chemical manufacture). Likewise, children whose birth mothers were occupationally exposed will not be eligible. This restriction applies to both the exposure and the referent group.

The cooperative agreement recipients' sites include communities whose drinking water was impacted by AFFF use at military bases or by industrial PFAS releases. Site selection considerations included the levels of PFAS drinking water concentrations at a site, the size of the population exposed, the experience of the researchers in conducting drinking water epidemiological studies, and geographic coverage. A key aim was to select sites so that a wide range in PFAS exposures levels were included in the study in order to enable the evaluation of exposure-response trends including effects at the lower and upper ranges of exposures. A ground water contaminant fate and transport model and a water system distribution model may be necessary to identify the areas with contaminated drinking water, determine the period when the drinking water was contaminated, and historically reconstruct PFAS drinking water concentrations.

Based on ATSDR's literature review of epidemiological studies of PFAS (ATSDR 2017), the study will examine associations between PFAS compounds and 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.

Sampling Methods: The Multi-site Study will be cross-sectional in design. If feasible, the recipient shall identify and enumerate all households served by the contaminated drinking water supply in the selected community in order to recruit potential participants to meet the sample size requirements for children and adults. If enumeration of all households is not feasible, then the recipient should consider non-probabilistic sampling approaches.

For sites with a contaminated public water supply, the recipient will request a list of residences served by the water purveyor (**Attachment 3c**). For sites with contaminated private wells, the

recipient will 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 (**Attachment 3d**).

Recruitment methods are described in the **Multi-site Study Protocol Section 3.5**. See further discussion in **Section A.2 of Supporting Statement A – Justification**.

Trained study staff will recruit, screen for eligibility, and enroll participants (**Attachment 4**). ATSDR assumes that 5 percent of the people who volunteer will not meet eligibility requirements. For purposes of annualized time and cost estimation, ATSDR assumes a 40 percent response rate across all sites.

Statistical sampling methods (e.g., a two-stage cluster sample) will 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 in order 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 should consider non-probabilistic sampling approaches such as “judgement” and “snowball” sampling approaches (Tyrer 2016).

Steps in screening are:

- Administer the eligibility screening scripts and schedule appointments (**Attachment 4**).
- Begin tracking the recruitment process (**Attachment 6**).
- Mail out appointment packets (**Attachment 7**), which will contain the following documents to keep and read before their appointments:
 - Appointment reminder cards (**Attachment 7a**), with instructions on how to prepare for the appointment
 - Informed consent packets (**Attachment 7b**),
 - Privacy Act Statement (**Attachment 7b1**)
 - Parental Permission and Child Assent Forms (**Attachment 7b2**)
 - Parental Consent to Release Student Information (**Attachment 7b3**)
 - Adult Consent Form (**Attachment 7b4**)
 - Parent/Child/Adult Permission for Medical Record Abstraction (**Attachment 7b5**)
 - Study Fact Sheet (**Attachment 7c**)
- Encourage participation with appointment reminder calls (**Attachments 8&9**).

B.2. Procedures for the Collection of Information

At the appointment, enrollment and data collection procedures are described in the **Multi-site Study Protocol Section 3.5.3, Section 3.6**, and in the Manual of Procedures for staff and contractor training (**Attachment 12**). Steps in enrollment are:

- Administration of informed consent, parental permission, and child assent (**Attachment 7b**).
- Update participant contact information, if needed (**Attachment 10**).
- Record participant medication list (**Attachment 11**).
- Take body and blood pressure measures (**Attachment 13**).
- Collect blood and urine biospecimens (**Attachment 14**).
- Administer questionnaire (**Attachment 15, 15a, 16**).
- (For children and parents) Administer the neurobehavioral test battery (**Attachment 18**).

After the appointment, ATSDR recipients will seek:

- Approval for medical record abstraction from medical office administrators (**Attachment 17**).
- Medical record verification for self-reported conditions noted in the questionnaire (**Attachment 17a-b**).
- Approval for education record abstraction from school administrators (**Attachment 18b**).
- Education record verification to compare to the results of the children's neurobehavioral assessments and their parents' assessments of their children (**Attachment 18c**).

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

The **Multi-site Study Protocol Section 3.3.1** describes the estimated number of eligible children and assumptions about participation rates needed to achieve statistical goals:

“For children, **Table 1** (and **Attachment 3a**) provide the sample size calculations for several health outcomes of interest assuming a type 1 (“ α error”) of .05 and type 2 error (“ β error”) of .20. It was considered important that a study have a total sample size so that exposures could be categorized into tertiles (i.e., reference, medium, and high) or preferably into quartiles (i.e.,

reference, low, medium and high). Per stratum estimates of needed sample size have been calculated based on different prevalence of outcomes and detected odds ratios or mean difference.

The proposed sample size of 2,000 children is large enough to effectively evaluate many of the health outcomes identified in the Pease Feasibility Assessment literature review and the recent systematic review (Rapazzo 2017) as potentially associated with PFAS in children. The health outcomes and biomarkers studied would include mean difference in total cholesterol (ranging from 156 to 637 per stratum), uric acid levels (556 per stratum), estimated glomerular filtration rate (eGFR; 275 per stratum), testosterone (about 400 per stratum) and insulin growth factor-1 (IGF-1; 146 per stratum). Based on our estimations, we would also be able to detect differences in risk for obesity and atopic dermatitis. A sample size of 2,000 children would be larger than many of the PFAS studies that evaluated neurobehavioral outcomes such as IQ and ADHD (Wang 2015, Stein 2013, 2014, Fei 2011, Hoffman 2010, Strom 2014).

An NHANES study of estimated glomerular filtration rate observed statistically significant findings with a total sample size of just under 2,000 children (Kataria 2015). For thyroid function, estradiol, delayed puberty, and asthma, a total sample sizes of 2,000 children may be sufficient, although larger sample sizes would be optimal (Lopez-Espinosa 2011, 2012; Stein 2016).

In summary, a total sample size of $\geq 2,000$ would be sufficient to evaluate a wide range of biomarkers and outcomes including lipids (and hypercholesterolemia), uric acid (and hyperuricemia), estimated glomerular filtration rate, testosterone, IGF-1, neurobehavioral measures (executive function, attention, IQ) and ADHD, rhinitis, and obesity.”

The **Multi-site Study Protocol Section 3.3.2** and **Attachment 3** describe the estimated number of eligible adults and assumptions about participation rates needed to achieve statistical goals:

“For adults, **Table 2** (and **Attachment 3b**) provide the sample size calculations for several health outcomes of interest assuming a type 1 (“ α error”) of .05 and type 2 error (“ β error”) of .20. In this exposure based study we assume an appropriate coverage of range of exposures that will enable stratification/categorization to tertiles or quartiles of exposure. Per stratum estimates of needed sample size (e.g. first vs. fourth quartile) have been calculated based on different measures of association such as odds ratios or detected mean difference.

The proposed sample size of 6,000 adults is large enough to effectively evaluate many of the health outcomes identified in the Pease Feasibility Assessment literature review. For example, for outcomes like elevated lipids levels (cholesterol) or uric acid, the range of 229 to 660 participants per stratum (i.e. quartile) or 200 to 550 per stratum, respectively, given observed differences would be needed. That would translate to overall sample size of about 800 to 2,600 participants being sufficient to detect differences at the specified level of precision and power (Steenland, 2009, 2010; Fisher 2013; Shankar 2011). Similar sample sizes would also be required to compare other common health outcomes such as cardiovascular disease (Shankar 2012). Larger sample sizes would be needed for liver function or osteoarthritis, with a total sample in the range of 3,000 to 4,000 subjects (Uhl 2013; Gallo 2012; Steenland 2010).

For thyroid disease and thyroid function, a total sample size of 6,000 may be sufficient although probably not optimal. However, NHANES studies of thyroid function and thyroid disease obtained statistically significant findings with total sample sizes considerably less than 6,000 (Melzer 2010; Wen 2013). NHANES studies of liver function also obtained statistically significant findings with total sample sizes considerably less than 6,000 (Gleason 2015; n=4333). For biomarkers of immune function (e.g., immunoglobulins, C-reactive protein and cytokines) and fatty liver disease, there was insufficient information to calculate sample sizes. However, a total sample size of 6,000 should be sufficient to evaluate these biomarkers as we assumed similar endpoint differences of those outcomes.

For ulcerative colitis, a sample size of 6,000 might be sufficient if the effect size in the C8 study (i.e., OR=3.05) was consistent for PFOA serum levels considerably lower than those in the C8 study. For more modest effect sizes (e.g., ORs < 2.75), a total sample size of 6,000 would not be adequate to evaluate associations with ulcerative colitis.

In addition, several epidemiological studies of adults exposed to PFAS that reported robust statistical associations with these health outcomes had smaller sample sizes than the one proposed for the Multi-site Study, e.g., NHANES studies (Nelson 2010, Wen 2013), a C8 longitudinal study (Fitz-Simon 2013), a C8 immune study (Looker 2014), and studies in China (Fu 2014) and Korea (Ji 2012).

In summary, a total sample size of $\geq 6,000$ in multi-site study should be sufficient to evaluate a broad range of biomarkers and outcomes such as lipids (and hypercholesterolemia), uric acid (and hyperuricemia), cardiovascular disease, osteoarthritis, immune biomarkers and biomarkers for fatty liver disease. It also may be sufficient to evaluate thyroid disease, thyroid function and liver function.”

In order to maximize participation in the Multi-site Study, ATSDR recipients will have the flexibility to schedule or re-schedule office or home visits within the study period (**Multi-site Study Protocol Section 3.5.3**).

- Interested recruits who are unable or unwilling to come to the study office, will be offered an in-home appointment by trained study staff to complete the study. Interested recruits who request or require a home interview, blood draw, and urine collection must reside within a one-hour drive from the study office.
- Study staff will give the interested recruit a reminder telephone call one to two days before the scheduled appointment (**Attachment 6**).
 - The study staff will make up to five contact attempts to an interested recruit who misses an appointment in order to reschedule the appointment and maximize the number of completed appointments (**Attachment 9**).

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

The **Multi-site Study Protocol** builds on activities undertaken in preparation of data collection for the ATSDR proof of concept research study currently being conducted of the Pease International Tradeport population (Portsmouth, NH) exposed to PFAS-contaminated drinking water (OMB Control No. 0923-0061). Several modifications to the **Multi-Site Study Protocol** and questionnaire were made based on these activities including:

- modification of the childhood neurobehavioral test battery to minimize burden,
- adjustment of the volume of blood to be collected from adults and children to ensure sufficient quantities for the clinical biomarker tests,
- modification of the childhood questionnaire,
- refinements to the medical records abstraction forms, and
- adaptation of the Pease data management system and community engagement strategy.

In addition, the protocol includes additional, quantitative bias analyses based on reviewer comments to the Pease Study protocol.

Some of the proposed data collection instruments for the Multi-Site Study have also been based on those successfully used in the “Anniston Community Health Survey: Follow up and Dioxin Analyses (ACHS-II)” (OMB Control No. 0923-0049; discontinued 11/12/2015) (**Attachments 10, 11, 13, 14**).

In the Pease Study, exposures to PFAS-contaminated drinking water occurred primarily at workplaces and day care centers at the Pease International Tradeport. Therefore, the Pease Study questionnaire has been modified for the Multi-Site Study to account for a likely different exposure scenario, i.e., drinking water exposures occurring primarily at the residence (**Attachments 15, 15a, 16**). The eligibility screeners (**Attachment 4**), medical records abstraction forms (**Attachments 17a, 17b**), and the school records abstraction form (**Attachment 18c**) are the same forms as those currently being used in the Pease Study.

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

B.5.1. Addressing Confounding and Co-exposure to Other Chemicals

The **Multi-site Study Protocol Section 3.10** and **Attachment 3** describe the statistical analyses and the methods to address confounding:

“ATSDR staff will perform statistical analyses with the participation of the recipients using SAS, R and STATA on the combined multi-site study dataset. ATSDR staff may also use SPSS for data management. ATSDR staff will calculate descriptive statistics (including means, geometric means, medians, standard deviations, and percentiles) to identify the presence and distribution of PFAS and effect biomarker analytes. Statistical methods will include multiple linear regression of continuous (untransformed and natural log transformed) effect biomarkers on continuous (untransformed and natural log transformed) PFAS serum levels and categorized PFAS serum levels, and logistic regression of categorized effect biomarkers (e.g., hypercholesterolemia) or disease prevalence on continuous (untransformed and natural log transformed) and categorical PFAS serum levels. ATSDR staff will use restricted cubic spline methods (or generalized additive models using cubic regression splines) for linear and logistic regression to obtain flexible, smoothed exposure-response curves. To identify risk factors that may act as confounders for a particular health outcome, the analysis will implement a “10% change in the estimate” rule (Maldonado 1993). It must be remembered that for any appreciable confounding to occur, the factor must be a strong risk factor for the outcome under consideration and must also be strongly correlated with the PFAS exposure under evaluation. For unmeasured risk factors, ATSDR proposed the use of negative controls and quantitative bias analyses (see below). These are all standard approaches for evaluating confounding by any risk factor including “co-exposures” by other environmental contaminants.

For example, evaluation of the confounding effects of smoking in occupational studies evaluating a chemical exposure and lung cancer typically observe only moderate confounding (e.g., between 20% and 30%, Blair et al. 2007). This is so even though smoking is an extremely strong risk factor for lung cancer and, at least in earlier occupational studies, typically was at least moderately associated with the chemical exposure or the exposed workforce. None of the diseases and clinical measures or neurobehavioral tests under evaluation in the Multi-site Study have a risk factor remotely as strong as smoking is for lung cancer. Although there are likely to be at least moderate correlations among the PFAS chemicals, confounding of one PFAS chemical by another PFAS chemical should be minor because it is not known that any are strong risk factors for any of the diseases or clinical measures or neurobehavioral tests under the study. (Nevertheless, we will evaluate whether a PFAS chemical confounds an association between another PFAS chemical and a disease or clinical measure by the 10% change-in-the-estimate rule mentioned above.) Moreover, it is very unlikely that any other (i.e., non-PFAS) chemicals or metals will be highly or even moderately correlated with PFAS chemicals. For example, correlations (Pearson correlation coefficient, R) between mercury and PFOA, PFOS, PFHxS and PFNA are consistently <0.20 among children in the NHANES data. In addition, lead and mercury are not very strong risk factors for any disease or clinical measure or neurobehavioral test – i.e., they are considerably weaker risk factors for health outcomes than smoking is for lung cancer.

Primary analyses will focus on estimated cumulative PFAS serum levels. Supplemental analyses will evaluate PFAS serum levels in the blood specimens obtained in the study as well as estimated maximum and average PFAS serum levels. The primary analyses will evaluate each PFAS chemical separately; sum of PFAS measures may also be considered. Statistical analyses

using prevalent cases in a cohort design which takes into consideration the times of diagnosis will also be conducted. ATSDR will explore the use of methods for evaluating multi-pollutant mixtures, such as the hierarchical Bayesian model, to analyze the effects of exposures to the PFAS mixtures. There are several caveats and recommendations in conducting analyses of mixtures to determine the optimal method that avoids amplifying bias due to confounding (Weisskopf et al 2018).

ATSDR will use quantitative methods to assess the impact of possible selection and information bias, as well as possible confounding due to unmeasured risk factors (Lash 2009). In addition, ATSDR will also identify “negative control” diseases with no known association with PFAS exposures to assess the impact of these potential biases (Lipsitch 2010). ATSDR conducted a literature search to identify these negative control diseases and included them in the questionnaire.

In summary, to gauge the potential and magnitude of possible selection bias and information biases, as well as confounding bias due to unmeasured risk factors, two approaches will be taken. First, quantitative methods described in Lash et al (2009) will be used to estimate the possible magnitude of selection and informational biases. Second, “negative control” diseases will be used to also estimate the potential and magnitude of these biases (Lipsitch et al 2010). Negative control diseases are those diseases not known to be associated with the exposures of interest. In the multi-site study, the exposures of interest are PFAS serum levels. The negative control diseases for children included in the questionnaire are celiac disease, scleroderma, lupus, and Crohn’s disease. In addition to these diseases, negative control diseases for adults include Parkinson disease, emphysema, chronic bronchitis, multiple sclerosis, and fibromyalgia.”

Table B.5.1.1. Personnel Consulted on Statistical Design

Name	Title	Affiliation	Phone	Email
Marian Pavuk, MD, PhD	Senior Epidemiologist, PI Multi-site Study	ATSDR	(770) 488-3671	fsh8@cdc.gov
Frank Bove, ScD, MS	Senior Epidemiologist, PI Multi-site Study	ATSDR	(770) 488-3809	fjb0@cdc.gov
Scott Bartell, PhD	Professor	University of California Irvine	(949) 313-4314	sbartell@uci.edu
David Savitz, PhD	Professor	Brown University	(401) 863-6090	david_savitz@brown.edu

In addition, the **Multi-site Study Protocol Section 2.4. General Approach for Study Recruitment** describes the sampling methods and recruitment strategies:

“All sites will fully document their methods and address how the final samples are likely to deviate from a true probability sample, drawing on relevant empirical data as feasible. Each site s will make adjustments as needed to attain the required study size per guidelines above and in coordination with ATSDR. Site investigators will work diligently to document all steps of the process and will commit to the technical oversight and quality control through the Sampling and Recruitment Working Group established from the Personnel Responsible for Collection and Analysis of Information (Supporting Statement B).”

ATSDR has established a Sampling and Recruitment Workgroup, comprised of the ATSDR and study sites investigators. The intent of the workgroup is to oversee technical evaluation for all sampling and recruitment methods to be applied in the multi-site study. As an integral part of the data collection and statistical analyses, this workgroup is a component of the previously proposed group under the “Personnel Responsible for Collection and Analysis of Information” and will serve multiple functions, including sharing information with ATSDR and across sites and overseeing initial sampling and recruitment efforts, as well as data collection and analyses to follow.

Table B.5.1.2. Personnel Responsible for Collection and Analysis of Information

Name	Title	Affiliation	Phone	Email
Marian Pavuk, MD, PhD	Senior Epidemiologist, PI Multi-site Study	ATSDR	(770) 488-3671	fsh8@cdc.gov
Frank Bove, ScD, MS	Senior Epidemiologist, PI Multi-site Study	ATSDR	(770) 488-3809	fjb0@cdc.gov
Michael Lewin, MS	Mathematical Statistician	ATSDR	(770) 488-3812	mdl0@cdc.gov
Scott Bartell, PhD	Site Principal Investigator	University of California Irvine	(949)313-4314	sbartell@uci.edu
John Adgate, MSPH, PhD	Site Principal Investigator	University of Colorado Denver	(303)724-4682	JOHN.ADGATE@CUANSCHUTZ.EDU
Laurel Schaider, PhD	Site Principal Investigator	Silent Spring Institute	(617)332-4288 ext 224	schaider@silentspring.org
Robert Laumbach, MD, MPH	Site Principal Investigator	Rutgers University	(848)445-6084	laumbach@eohsi.rutgers.edu
Linda Brown, MPH, DrPH	Site Principal Investigator	Research Triangle Institute	(301)816-4626	lindabrown@rti.org

Erin Bell, PhD	Site Principal Investigator	State University of New York Albany	(518)402-0375	ebell@albany.edu
Kory Groetsch, MS	Site Principal Investigator	Michigan Dept of Health and Human Services	(517)335-8350	GroetschK@MICHIGAN.GOV

B.5.2. Working Groups to Oversee Modeling Quality Control

ATSDR will establish working groups to oversee thorough technical evaluation and quality assurance and quality control (QA/QC) for all methods and models in the historical reconstruction of groundwater resources and distribution of drinking water and for all PK/PBPK models used for historical serum reconstruction. These groups will serve multiple functions such as sharing information with ATSDR and across sites and overseeing quality control. Site visits, and if needed audits of modeling data at each site will be part of those efforts.

The recipients are required to estimate historical PFAS concentrations for both drinking water and serum. The required level of precision will be agreed upon by the site investigators as well as discussion of measurement variability, limits of detections etc. and the criteria for determining the precision of the serum concentration estimates without using the drinking water data

These working groups are comprised of technical experts specific to the type of modeling (e.g., the serum reconstruction QA/QC working group has experts in PBPK modeling). These groups also include ATSDR personnel and contractors that are already involved in the project. To improve cross-agency communication and awareness, ATSDR will also include members of other agencies that have an interest in PFAS (e.g., EPA).

There will be annual site-visits by the working groups and bi-monthly conference calls to facilitate any QA/QC-related activities and information exchanges. Ad-hoc calls or visits by ATSDR or working groups to address emerging issues at sites as needed will be arranged with site investigators.

Each recipient will submit a report detailing the historical reconstruction and PBPK modeling efforts; these reports will be externally peer-reviewed per the CERCLA mandate and the Information Quality Bulletin.

Table B.6.1. Personnel Responsible for Quality Assurance and Quality Control for Historical Reconstruction of Groundwater Resources and Distribution of Drinking Water

Name	Title	Affiliation
Rene Suarez-Soto, EIT, MS	Workgroup Chair	ATSDR
Jason Sautner, MSCE	Member	ATSDR
John Adgate, MSPH, PhD	Site Principal Investigator	University of Colorado Denver
Chris Higgins MS, PhD	Member	Colorado School of Mines
Russell Detwiler, PhD	Member	University of California Irvine
Scott Bartell, PhD	Site Principal Investigator	University of California Irvine
Ted Lillys, P.E	Member	Research Triangle Institute
Laurel Schaidler, PhD	Site Principal Investigator	Silent Spring Institute
Panos Georgopoulos, PhD	Member	Rutgers University
Steve Shost, PhD, MPH	Member	New York State Department of Health
Kory Groetsch, MS	Site Principal Investigator	Michigan Department of Health and Human Services
Jordan Bailey, MS, PhD	Site Co-Principal Investigator	Michigan Department of Health and Human Services
Joost Vant Erve, PhD	Member	Michigan Department of Health and Human Services

Table B.6.2. Personnel Responsible for Quality Assurance and Quality Control for PK/PBPK Models Used for Historical Serum Reconstruction

Name	Title	Affiliation
Rachel Rogers, PhD	Workgroup Chair	ATSDR
Clement Welsh, PhD	Member	ATSDR
John Adgate, MSPH, PhD	Site Principal Investigator	University of California Irvine
Anne Starling, PhD	Co-Principal Investigator	University of California Irvine
Scott Bartell, PhD	Principal Investigator	University of California Irvine
Timothy Fennell, PhD	Member	Research Triangle Institute
Laurel Schaidler, PhD	Principal Investigator	Silent Spring Institute
Panos Georgopoulos, PhD	Member	Rutgers University
Steve Shost, PhD, MPH	Member	New York State Department of Health
Andrea Candara, MS	Member	New York State Department of Health
Kory Groetsch, MS	Site Principal Investigator	Michigan Department of Health and Human Services
Jordan Bailey, MS, PhD	Site Co-Principal Investigator	Michigan Department of Health and Human Services
Joost Vant Erve, PhD	Member	Michigan Department of Health and Human Services

References

Agency for Toxic Substances and Disease Registry (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

Blair A, Stewart P, Lubin JH, Forastiere F. Methodological issues regarding confounding and exposure misclassification in epidemiological studies of occupational exposures. *Am J Ind Med.* 2007 Mar;50(3):199-207.

Lash TL, Fox MP, Fink AK. *Applying Quantitative Bias Analysis to Epidemiologic Data.* Springer (NY, 2009).

Lipsitch M, Tchetgen Tchetgen E, Cohen T. Negative controls: A tool for detecting confounding and bias in observational studies. *Epidemiol* 2010;21:383-388.

Weisskopf MG, Seals RM, Webster TF. Bias Amplification in Epidemiologic Analysis of Exposure to Mixtures. *Environ Health Perspect* 2018;126:047003.

Tyrer S, Heyman B. Sampling in epidemiological research: issues, hazards and pitfalls. *BJPsych Bull.* 2016;40(2):57-60.

List of Appendices

Appendix A. Authorizing Legislation

Appendix B. 60-day Federal Register Notice

Appendix B1. Public Comments and Program Responses

Appendix C. Notice of Funding Opportunity (NOFO)

Appendix D. ATSDR Pease Feasibility Assessment

Appendix E. Privacy Impact Assessment

Appendix F. IRB Approval Memo

Appendix G. Data Sharing and Disclosure Review

Multi-site Study Protocol and Attachments

Attachment 1. Investigators and Key Study Personnel

Attachment 2. Biochemical Analytical Plan in Children and Adults

Attachment 3. Justification for Sample Size Calculations

Attachment 3a. Sample Size for Child Study

Attachment 3b. Sample Size for Adult Study

Attachment 3c. Drinking Water Information Collection Request Form (Water Purveyors)
Attachment 3d. Drinking Water Information Collection Request Form (Environmental Protection Agencies)

Attachment 4. Eligibility Screening Script

Attachment 5. Recruitment Materials

Attachment 6. Recruitment Tracking Form

Attachment 7. Appointment Packet

- Attachment 7a. Appointment Reminder Card
- Attachment 7b. Informed Consent Packet
 - Attachment 7b1. Privacy Act Statement
 - Attachment 7b2. Parental Permission and Child Assent Forms
 - Attachment 7b3. Parental Consent to Release Student Information
 - Attachment 7b4. Adult Consent Form
 - Attachment 7b5. Parent/Child/Adult Permission for Medical Record Abstraction
- Attachment 7c. Study Fact Sheet

Attachment 8. Appointment Reminder Telephone Script

Attachment 9. Appointment Tracking Form

Attachment 10. Update Contact Information Hardcopy Form

Attachment 11. Medication List

Attachment 12. Manual of Procedures

Attachment 13. Body and Blood Pressure Measures Form

Attachment 14. Blood Draw and Urine Collection Form

Attachment 15. Child Questionnaire – Long Form

- Attachment 15a. Child Questionnaire – Short Form

Attachment 16. Adult Questionnaire

Attachment 17. Request for Medical Record Abstraction

- Attachment 17a. Medical Record Abstraction Form - Adult
- Attachment 17b. Medical Record Abstraction Form - Child

Attachment 18. Child/Parent Neurobehavioral Test Battery

- Attachment 18a. NBT Time Estimation Table, by Age in Years
- Attachment 18b. Request for Child School Record Abstraction
- Attachment 18c. Child School Record Abstraction Form

Attachment 19. Body and Blood Pressure Measurements Report

Attachment 20. Advance Reporting Script for Clinical Tests

- Attachment 20a. Advance Clinical Test Report Tracking Form
- Attachment 20b. Letter Report of Critical Values

Attachment 21. Clinical Test Results Report

Attachment 22. PFAS Results Report

- Attachment 22a. ATSDR PFAS Factsheet

