

Centers for Disease Control and Prevention

National Center on Birth Defects and Developmental Disabilities Extramural Research Program Office

Characterizing the Natural History of Fragile X Syndrome to Inform the Development of Intervention Outcome Measures

RFA-DD-21-002

Application Due Date: 01/11/2021

Characterizing the Natural History of Fragile X Syndrome to Inform the Development of Intervention Outcome Measures

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Part 1. Overview Information

Participating Organization(s)

Centers for Disease Control and Prevention

Components of Participating Organizations

National Center on Birth Defects and Developmental Disabilities

Notice of Funding Opportunity (NOFO) Title

Characterizing the Natural History of Fragile X Syndrome to Inform the Development of Intervention Outcome Measures

Activity Code

U01, Research Project - Cooperative Agreement

Notice of Funding Opportunity Type

New

Agency Notice of Funding Opportunity Number

RFA-DD-21-002

Assistance Listings (CFDA) Number(s)

93.073

Category of Funding Activity:

Health

NOFO Purpose

The purpose of this NOFO is to build on the foundation of the Fragile X Online Registry With Accessible Research Database (FORWARD) to conduct research to better characterize the natural history of fragile X syndrome (FXS) and meaningful outcome measures to improve the lives of children and adolescents with FXS with and without autism spectrum disorder (ASD), and from different racial/ethnic groups and geographic locations across the United States. The research will characterize the cognitive, behavioral, and adaptive skills, and other indicators of functioning of individuals with FXS. Also of interest are cognitive, behavioral, and adaptive skills outcomes for individuals with FXS as a function of diagnostic history, early intervention, and access to services. Finally, this study will explore the practical, financial, and psychological impact that caring for a family member with FXS has on caregivers and siblings of those with FXS. Planned post-award coordination of standardized in-person behavioral and functional assessments and follow-up telephone survey questionnaires with CDC's Study to Explore Early Development (SEED) Follow-up Study (RFA-DD-21-001) will facilitate comparison of health and functional outcomes for the FXS population with those for other related and frequently co-occurring conditions, such as ASD and developmental delay.

Key Dates

Publication Date:

To receive notification of any changes to RFA-DD-21-002, 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:	**12/07/2020**
Application Due Date:	**01/11/2021**

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:	**03/29/2021**
Secondary Review:	**05/18/2021**
Estimated Start Date:	**09/01/2021**
Expiration Date:	**01/12/2021**
Due Dates for E.O. 12372:	**Executive Order 12372 does not apply to this program.**

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 25 pages.

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

Pages that exceed page limits described in this NOFO will be removed and not forwarded for peer review, potentially affecting an application's score.

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

Executive Summary

- **Purpose.** The purpose of this NOFO is to build on the foundation of the Fragile X Online Registry With Accessible Research Database (FORWARD) to conduct research to better characterize the natural history of fragile X syndrome (FXS) and meaningful outcome measures to improve the lives of children and adolescents with FXS with and without autism spectrum disorder (ASD), and from different racial/ethnic groups and geographic locations across the United States. The research will characterize the cognitive, behavioral, and adaptive skills, and other indicators of functioning of individuals with FXS. Also of interest are cognitive, behavioral, and adaptive skills outcomes for individuals with FXS as a function of diagnostic history, early intervention, and access to services. Finally, this study will explore the practical, financial, and psychological impact that caring for a family member with FXS has on caregivers and siblings of those with FXS. Planned post-award coordination of standardized in-person behavioral and functional assessments and follow-up telephone survey questionnaires with CDC's Study to Explore Early Development (SEED) Follow-up Study (RFA-DD-21-001) will facilitate comparison of health and functional outcomes for the FXS population with those for other related and frequently co-occurring conditions, such as ASD and developmental delay.
- **Mechanism of Support.** Cooperative Agreement
- **Funds Available and Anticipated Number of Awards.** The estimated total funding (direct and indirect) for the entire period of performance for this NOFO is $4,000,000. The estimated total funding (direct and indirect) for Year 1 of this NOFO is $800,000. Awards issued under this NOFO are contingent upon availability of funds and a sufficient number of meritorious applications. A single award of an estimated $800,000 for year 1 is anticipated if applicants propose recruiting study participants from a group of clinics to achieve the overall study minimum sample size of 600 participants over the entire period of performance. Applicants may alternatively propose to recruit from a single clinic, in which case the award would reflect the proportionate proposed sample size. For example, if an applicant proposes to recruit 360 participants over the period of performance (i.e., 60% of the total sample needed for this study), the award ceiling would be approximately 60% of the total available funding. Five to seven smaller awards of an estimated $150,000 for year 1 are anticipated if applicants propose recruiting a smaller sample from an individual clinic. Because the scope of the proposed research may vary from application to application, it is also anticipated that the size of 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.

- **Budget and Period of Performance.** The estimated total funding (direct and indirect) for the first budget period, 09/01/2021 to 08/31/2022, is $800,000. The estimated total funding (direct and indirect) for the entire period of performance, 09/01/2021 to 08/31/2026, is $4,000,000.
- **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 does not make awards to individuals directly. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply.
- **Number of PDs/PIs.** Applications may include more than one PI; however, the first PI listed on the application will be the contact PI for all correspondence. Any additional PIs are permitted but would be referred to as Co-PIs.
- **Number of Applications.** Only one application per institution (normally identified by having a unique DUNS number) will be accepted.
- **Application Type.** New
- **Special Date(s).** N/A
- **Application Materials.** See **Section IV.1** for application materials

Part 2. Full Text

Section I. Funding Opportunity Description

Statutory Authority

This program is authorized under Sections 301 and 317 C of the Public Health Service Act (42 USC Sections 241 and 247b-4), as amended.

1. Background and Purpose

Background

What is fragile X syndrome?

Over the past two decades, scientists have made advancements in understanding fragile X syndrome (FXS), a genetic disorder caused by changes in a gene that scientists called the fragile X mental retardation 1 (*FMR1*) gene when it was first discovered. FXS is the most common known inherited cause of intellectual disability (ID). FXS affects both males and females. However, females often have milder symptoms than males. The exact number of people who have FXS is unknown, but a review of research studies estimated that about 1 in 7,000 males and about 1 in 11,000 females have been diagnosed with FXS. [1] People who have FXS can present with a range of ID [2] and may also experience a wide range of emotional, behavioral,

[3] sensory, and/or social difficulties. [4] A notable proportion of people with FXS have been diagnosed with autism spectrum disorder (ASD), although the variability of estimates is wide ranging, from 30%-67% in males and 16%-23% in females with FXS. [5, 6, 7] FXS is characterized by mild-to-moderate ID, autistic behaviors, sensory integration problems, and physical features, such as long face and large prominent ears. FXS causes a range of developmental problems including learning disabilities and cognitive impairment. Over the past two decades, scientists have made advancements in understanding the genetics of FXS: it is a genetic disorder caused by a CGG trinucleotide repeat mutation in the *FMR1* gene. In people with FXS, the CGG segment is repeated more than 200 times, while in people without FXS, it repeats from 5 to about 40 times.

What is FORWARD?

CDC has funded three studies to expand our understanding of FXS. The Fragile X Online Registry With Accessible Research Database (FORWARD) was developed and implemented to support collection and management of longitudinal data on individuals with FXS, incorporating the earlier-developed FXS Registry. There are two main components to FORWARD: (1) the registry, which collects primarily demographic information from families with FXS-associated disorders (full mutation, premutation, and noncarriers) and (2) the longitudinal database, which collects data from individuals with full mutation FXS by clinicians, primarily during a patient?s scheduled clinic visit, and by parents/caregivers.

The first study (CDC-RFA-DD-07-003; 2008 to 2011) piloted an infrastructure to conduct a study on FXS across multiple sites located in geographic regions across the United States. The Fragile X Clinical and Research Consortium (FXCRC), consisting of over 25 FXS specialty clinics, was successful in collecting data across multiple sites. This first study showed that using a consortium of clinics was an effective way to engage multiple clinics. Evaluation of data collection forms led to revisions agreed upon by members of the FXCRC, the FORWARD project staff, and CDC collaborators during that study period.

The second study (CDC-RFA-DD-11-007; 2011 to 2015) developed and piloted the infrastructure for a registry and for longitudinal data collection. [8] The goal of the registry was to develop a source of potential participants for FXS-related research conducted by CDC or by others. The longitudinal dataset was designed to support collection and analysis of data over time on a large cohort of individuals with FXS, a notable challenge given the prevalence of FXS. The most significant accomplishment of the second study was the successful creation of the infrastructure for investigators to coordinate with specialty clinics in the FXCRC to contribute longitudinal data to FORWARD. Building on this infrastructure will enhance understanding of FXS and its co-occurring conditions, to describe current services and their impact on outcomes and quality of life, and to identify service needs and barriers.

The third study (CDC-RFA-DD-15-003; 2015 to 2020) is ongoing and aims to build on the foundation created via the first two studies by providing information to guide parents and health professionals towards the best services and supports possible, as well as inspire future research questions. During the third study, FORWARD was expanded to include data from adults with FXS on co-occurring conditions as well as data on health care transition, health monitoring, vocational and educational status, and other areas that affect

quality of life. Three clinics also received additional support to engage racial/ethnic minority and underserved populations and test ways to measure developmental changes in cognition, behavior, emotion, and neurobiology in the population affected by FXS. Following the third study, a supplemental year awarded in 2020 allows for continued data collection from individuals already enrolled in the longitudinal database and from new participants to increase sample size for future analyses.

What has FORWARD accomplished?

Results from FORWARD published in recent years include publications related to symptoms, functioning, and co-occurring conditions of FXS. Kaufmann and colleagues [7] used data collected from 2012 to 2014 to find that over half of males met the diagnostic criteria for ASD and that the group with co-occurring ASD and FXS had higher prevalence of seizures, sleep problems, and behavior problems than those without co-occurring ASD. Additionally, an investigation using FORWARD data on the psychometric properties of the Social Communication Questionnaire and Social Responsiveness Scale in predicting an ASD diagnosis indicated that these instruments have limited use in this population. [9] The authors' proposal of adapted versions of these scales for characterizing ASD in the population affected by FXS added knowledge about outcomes measurement among individuals with FXS. Another analysis of FORWARD data about preventive healthcare services suggested that most children with FXS meet dental care and immunization but not physical activity guidelines, particularly individuals with co-occurring ASD. [10] More recent publications from the third study described bowel and bladder training [11] and irritability/aggression/agitation/self-injurious (IAAS) behaviors among individuals with FXS. [12]

Which gaps in FXS knowledge will this NOFO address?

Although data collected in FORWARD advanced knowledge about FXS, its co-occurring conditions, and outcomes, gaps remain in the characterization of health and functional outcomes in association with medical care, education services, and support for transition across the lifespan. We are just beginning to understand how this complex condition affects individual developmental trajectory, how this condition affects individuals with FXS across the lifespan, the impact of FXS and co-occurring ASD, and how we can design early interventions to improve the lives of all of those affected. Data are also limited concerning the prevalence of other conditions co-occurring with FXS, such as attention-deficit/hyperactivity disorder (ADHD), anxiety, depression, and seizures. In addition, data are limited on the frequency of interventions used to treat symptoms, [13, 14] effectiveness of interventions, and receipt of health services among people with FXS. Research leading to a greater understanding of the unmet needs and challenges faced by individuals who have FXS could potentially benefit all individuals affected by intellectual disabilities.

To address these gaps, this NOFO will conduct longitudinal follow-up studies of individuals with FXS previously enrolled in FORWARD as well as enroll and collect data from new participants who receive care in FXS specialty clinics. In addition, this NOFO, in combination with the CDC's Study to Explore Early Development (SEED) follow-up study (RFA-DD21-001), will address gaps in understanding how outcomes and needs differ between individuals with FXS and individuals with ASD who do not have FXS during early childhood to young adulthood and beyond. [15]

Purpose

The purpose of this NOFO is to build on the foundation of FORWARD to conduct research to better understand the natural history of FXS and identify meaningful outcome measures to improve the lives of children and adolescents with FXS with and without ASD and among different racial/ethnic groups and geographic locations across the United States. This research will characterize the cognitive, behavioral, and adaptive skills, and other indicators of functioning of individuals with FXS. Also of interest are cognitive, behavioral, and adaptive skills outcomes for individuals with FXS as a function of diagnostic history, early intervention, and access to services. Finally, this study will explore the practical, financial, and psychological impact that caring for a family member with FXS has on caregivers and siblings of those with FXS. Planned post-award coordination of standardized in-person behavioral and functional assessments and follow-up telephone survey questionnaires with CDC's SEED Follow-up Study will facilitate comparison of health and functional outcomes for the FXS population with those for other related and frequently co-occurring conditions, such as ASD and developmental delay.

Healthy People 2030 and other National Strategic Priorities

The National Center on Birth Defects and Developmental Disabilities (NCBDDD) of CDC within HHS is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2030" and to measuring program performance as stipulated by the Government Performance and Review Act (GPRA). Specifically, this NOFO addresses the following Healthy People 2030 Goals:

- DH-2030-5 Reduce the proportion of adults with disabilities who experience serious psychological distress
- AH-2030-R2 Increase the proportion of students who are served under the Individuals with Disabilities Education Act (IDEA) who graduate high school with a diploma
- MHMD-2030-D1 Increase the number of youths with serious emotional disturbance (SED) who are identified and receive treatment
- MICH-2030-19 Increase the proportion of children and adolescents with special health care needs who receive care in a family-centered, comprehensive, and coordinated system

Public Health Impact

FXS, one of the most common causes of inherited ID, is a lifelong condition that affects individuals, families, and health and education systems. By addressing gaps in knowledge about the health status of people living with FXS and effects of services, this research supports the long-term goal of improving health outcomes and quality of life among people with FXS. Specifically, information about cognitive, behavioral, and developmental outcomes for individuals with FXS can provide a more complete epidemiologic profile of the FXS population to inform development and enhancement of interventions and services. Data collected through this NOFO is intended to improve the health, functioning, and quality of life among persons with FXS and their families by

1. improving our understanding of the relationship between earlier diagnosis, services received, and later cognitive, behavioral, and adaptive function;
2. informing the development of outcome measures for future drug treatment trials; and
3. informing public policies on eligibility for services.

Relevant Work

As indicated above, this NOFO will build on three multi-year studies. The first pilot study (2008 to 2011) tested the infrastructure required to implement multi-site research in FXS, the Fragile X Clinical and Research Consortium (FXCRC). The second pilot study (2011 to 2015) tested the feasibility of longitudinal data collection across these multiple FXS specialty clinics. During that study, FXS specialty clinics across the country, in collaboration with the FXCRC, contributed data on individuals diagnosed with FXS, from birth to 24 years of age. Data are currently being collected through FORWARD by 24 participating clinics, each with local IRB approval, using structured clinician and parent-report forms and standardized parent-report instruments on behavior and communication (i.e. SRS, SCQ, ABC-C). The third study (2015 to 2020) continued the work established in the pilot studies, expanding data collection for FORWARD and enabling longitudinal data collection for existing and new participants. That study also emphasized the enrollment of minority and underserved populations and adults with FXS over 24 years of age. Items in the registry were revised and questions relating to the health and quality of life of adults with FXS were added.

In addition to building on prior investments in FORWARD, this NOFO will leverage the infrastructure and the methods used in the SEED follow-up study (RFA-DD-21-001). SEED is an ongoing multi-phase, multi-site, case control study of children identified at age 2 to 5 years with ASD, other developmental disabilities and from the general population. SEED was originally conducted in three phases among children in three birth cohorts, i.e., children born 2003 to 2006, 2008 to 2012, and 2014 to 2017, and is ongoing through July 2021. As part of the SEED follow-up study, in 2021 to 2026, longitudinal follow-up and research on previous SEED participants will obtain information through early adulthood on their health and functioning, service use and needs, and the impact of ASD on their families. Similarity of methods of this FXS study with that in the SEED follow-up study will improve efficiency and consistency of data collection on cognitive, behavioral, adaptive skills, and other indicators of functioning for individuals with FXS with or without ASD. This cross-program coordination will increase understanding of differences in functioning, outcomes, diagnostic history, early intervention and service needs for children with FXS with and without ASD, and children with ASD without FXS in similar age groups from childhood through young adulthood.

2. Approach

The work specified in this NOFO will build on FORWARD and include an even stronger focus on addressing gaps in knowledge identified from stakeholders and FXS experts, i.e., enhancing the understanding of cognitive, behavioral, adaptive skills and other indicators of functioning of individuals with FXS with and without autism spectrum disorder (ASD) and among different racial/ethnic groups and geographic locations.

Specifically, this NOFO includes collection of longitudinal cognitive, developmental, behavioral, clinical, and environmental data to accomplish the following:

- describe the health and functioning of individuals with FXS during childhood, adolescence, and young adulthood;
- inform our understanding of the relationship between earlier diagnosis and intervention and later cognitive/behavioral functioning;
- analyze the impact of treatments and interventions on health outcomes and quality of life; and
- improve approaches to measuring cognitive and behavioral status in patients with FXS.

Required Elements

- *Computer Assisted Telephone Interviews (CATI).* Each site is expected to share contact information of consented caregivers with a CDC contractor (one contractor for all of the FXS and SEED research sites). The contractor will conduct follow-up CATI with parents or caregivers.
- *Standardized assessments.* This NOFO will capitalize on the data already collected via FORWARD, to include new data from standardized assessments to characterize the cognitive, behavioral, and adaptive skills, and other indicators of functioning of individuals with FXS born between 2003 and 2017 (inclusive). Each site is expected to conduct in-person, standardized assessments and enter data for those assessments into a secure, contractor-developed data transmission site. Each site is expected to also make the data available directly to CDC upon request.
- *Coordination with SEED.* Planned coordination of the selection of standardized in-person assessments and telephone survey questionnaires with SEED Follow-up Study (RFA-DD-21-001) will facilitate comparison of health and functional outcomes for the FXS population as compared to individuals in the general population and individuals with other related and frequently co-occurring conditions, such as ASD without FXS, and developmental delay (DD). Sites are expected to collaborate with other recipients, CDC, and SEED Follow-up Study recipients to determine the list of in-person and CATI assessments that will be administered.

Structure of Study

This NOFO will support an observational, longitudinal study on individuals with full mutation FXS aged 5 to 23 years who have previously participated in FORWARD data collection and new participants who did not previously participate in FORWARD. This study is expected to engage and complete data collection for at least 150 eligible participants each of the four years of data collection in this NOFO for a minimum of 600 participants over the 5-year project period. Although FORWARD provides a potential source of eligible participants aged 5 to 23 years for the current NOFO, investigators may also recruit new participants.

Applicants may propose recruiting study participants from an individual clinic or recruiting from a group of clinics with which the principal investigator has documented data sharing and collaborative agreements. Recipients are expected to coordinate and collaborate with the CDC and CDC contractor to ensure timely and accurate data collection. Recipients can collaborate with the FXCRC to facilitate access to study participants from the FXS specialty clinics. Additionally, recipients are expected to participate in FXS meetings, conference calls, and workgroups to provide individual input and advice on research gaps in risk factors for FXS and

the characteristics and needs of children with FXS that can be addressed using existing FORWARD data.

Recruitment of equal numbers of individuals across three birth cohorts with years similar to those for the SEED participants (i.e., individuals born 2003 to 2007, 2008 to 2012, and 2013 to 2017) will maximize statistical power for comparative analyses across studies. Applications for the full budget ceiling amount are expected to enroll, assess, and complete data collection (including telephone interviews) for a minimum of 150 individuals each of the 4 years of data collection in this NOFO, equally divided among the three birth cohorts. Applications for lower budget amounts are expected to enroll, assess, and complete data collection on a proportionate sample size (e.g., if requesting 60% of the funding ceiling, applicants are expected to enroll, assess, and complete data collection on a minimum of 90 individuals each year) to ensure the overall NOFO aims of complete data on at least 150 participants each year, a minimum of 600 participants over the project period.

Study Requirements:

1. Obtain institutional review board (IRB) approvals or reliances, and site-specific consent forms, as required based on the new common rule for a single IRB, and assist CDC in submitting an information collection request to the Office of Management and Budget for approval in Year 1 to share standardized assessment data from participants and personally identifiable, individual-level contact information of consented caregivers of all participants from each clinic with a central CDC contractor.
2. In Year 1, collaborate with CDC and a CDC contractor to develop, test, and use secure electronic data systems for sharing participant information, assessments, and conducting interviews.
3. Hire, train, and maintain clinic personnel. Recipients are expected to hire an investigator qualified to train and standardize psychometrists in each clinic enrolling participants, determine their field readiness, evaluate administration fidelity and scoring reliability, and answer questions from participants and families.
4. Enroll and maintain contact with participants. Enrolled participants are expected to be evenly split across the three birth cohorts. Recipients are expected to share the caregiver contact information with a CDC-funded contractor responsible for conducting telephone interviews and collaborate with CDC and the CDC contractor to achieve the minimum sample size for the overall study (i.e., at least 600 participants with CATI and standardized assessment data across the period of data collection, distributed equally across three birth cohorts).
5. Recipients will be expected to implement and provide data on the success of strategies to maximize enrollment of FORWARD and new participants within each clinic as well as maintain contact with study participants. Strategies should emphasize enrollment and retention of participants of diverse race/ethnicity and demographic backgrounds.
6. Conduct in-person standardized assessments. Recipients are expected to administer standardized psychometric assessments with participants with full-mutation FXS born between 2003 and 2017 (inclusive), who are already enrolled in FORWARD, or are new enrollees. They must employ staff for scheduling, obtaining informed consent and administering a standardized psychometric assessment of approximately 90 minutes in length.
7. Generate and provide feedback letters. Recipients are expected to provide caregivers

who desire feedback with feedback on results of the psychometric assessment by sending a standardized letter to participants within one month of the assessment.
8. Maintain confidentiality of study documents and contribute site-specific data to a pooled dataset. Recipients are expected to store, enter, and transmit relevant data in a standardized and secure manner with common elements mutually agreed upon by CDC and recipients. This will become part of a pooled dataset that will be maintained and overseen by CDC and a CDC contractor and accessed by recipients and clinic sites through a CDC-approved mechanism that meets Federal standards for security and confidentiality.
9. During the participant enrollment and data collection period, share participant contact information with the CDC-funded contractor that will be conducting the follow-up telephone survey questionnaire. Recipients are expected to securely share personally identifiable, individual-level contact information of consented caregivers with the CDC contractor for CATI on a biweekly basis.
10. Serve as the point of contact for interested and enrolled participants throughout implementation of the follow-up surveys; work collaboratively with CDC's survey contractor to maximize participation. Recipients are expected to meet by phone or video call with CDC's central interviewing contractor on a biweekly basis to discuss study progress and troubleshoot any problems with study implementation.
11. Collaborate with other recipients, CDC, and CDC-funded recipients of the SEED Follow-up Study (RFA-DD-21-001). Recipients are expected to collaborate with other recipients and CDC to discuss and determine the list of in-person and CATI assessments that will be finalized during the first year of the cooperative agreement.
12. Collaborate with clinicians and researchers from the sites participating in the longitudinal database and CDC representatives to identify important clinical care and public health research questions and utilize data from the longitudinal database to address them.
13. Collaborate with the other recipients and CDC representatives to establish and implement guidelines and processes for data analysis and publications.
14. Complete at least two manuscripts submitted for publication each year in years 2 through 5 of this NOFO as first or co-author using previously collected FORWARD data and/or data collected under the current agreement. Manuscripts are expected to be prepared and submitted in accordance with guidelines and processes established in collaboration with CDC and other recipients.
15. Participate in a Steering Committee to encourage collaboration across recipients of this NOFO and provide the necessary expertise and oversight to ensure successful completion of the objectives.

Objectives/Outcomes

Overall Study Objectives:

1. To ensure data collected are of high scientific quality and comparable to other sites by following a common methodology established with CDC and other recipients.
2. To implement methods to ensure high participation rates of previous FORWARD participants as well as new participants and maximize the number of completed surveys and in-person assessments.

3. To collect and analyze standardized, high-quality information via parental or caregiver (or participant) telephone interviews and in-person assessments to inform further research and improve key outcomes for individuals with FXS and their families across geographically diverse participating FXS clinics.
4. To interpret and disseminate analytic results to expand the evidence base that can inform research and public health action.

Expected Outcomes:

1. Produce timely, high-quality, longitudinal, standardized data on cognitive, behavioral, and adaptive skills outcomes for individuals with FXS, with and without ASD and among different racial/ethnic and geographic groups, and contribute to a common research database that will facilitate the following research goals:
    a. Characterize the cognitive, behavioral, and adaptive functioning of individuals with FXS
    b. Investigate differences in current cognitive, behavioral, and adaptive functioning as a function of earlier indicators (e.g., age at diagnosis and intervention, and access to services)
    c. Investigate the relationship between earlier diagnosis and intervention, and later cognitive, behavioral, and adaptive functioning
    d. Characterize the sequencing and circumstances of FXS diagnosis and other mental, developmental, and behavioral diagnoses
    e. Characterize the practical, financial, and psychological impact of FXS on caregivers and siblings
    f. Characterize FXS from childhood to young adulthood
2. Analyze and disseminate data on individuals with FXS and their families to better characterize the natural history of FXS and meaningful outcome measures to improve the lives of children, adolescents, and young adults with FXS with and without ASD and their families.

Target Population

The target population is comprised of individuals with a diagnosis of full mutation FXS who visit FXS specialty clinics, who were born between 2003 and 2017 (inclusive), and represent the racial/ethnic diversity of the population in the FXS clinic catchment area. This study is expected to engage and complete data collection for at least 150 eligible participants each of the four years of data collection in this NOFO for a minimum of 600 participants over the 5-year project period. Applications for the full budget ceiling amount are expected to enroll, assess, and complete data collection on a minimum of 150 individuals each of the four years of data collection in this NOFO, approximately equally divided among the three birth cohorts. Applications for lower budget amounts are expected to enroll, assess, and complete data collection on a proportionate sample size (e.g., if requesting 60% of the funding ceiling, applicants are expected to enroll, assess, and complete data collection on a minimum of 90 individuals each year), to ensure the overall NOFO aims of at least 150 participants each year and a minimum sample size of 600 participants. Participants can be those who have previously contributed to FORWARD or are new to the study, with clinics encouraged to first recruit previous FORWARD participants. Applicants are encouraged to recruit from populations that

are diverse with respect to racial/ethnic groups, socioeconomic status, and other indicators of health disparities to represent their clinic population. Applicants will be expected to identify, establish, or extend partnerships with clinics or organizations that serve individuals with FXS, in order to support data collection, translation and dissemination of study findings.

Collaboration/Partnerships

Recipients will be expected to collaborate with CDC, a CDC survey and data center contractor, and other FXS and SEED recipients to accomplish the data collection and other goals and objectives stated in this NOFO. All recipients will be expected to participate in workgroups with CDC and other recipients to discuss and finalize data collection instruments.

Recipients will be expected to contribute their site-specific individual participant data to a shared data pool for potential analysis by FXS investigators, SEED investigators, and CDC. For this purpose, they will be expected to adhere to the following:

1. Clinic-specific roles and responsibilities for maintaining the confidentiality and security of the personally identifiable information collected as part of this research; and
2. CDC-approved mechanisms for accessing pooled, de-identified data through a CDC-approved remote access system meeting Federal standards for maintaining security and confidentiality of participant data.

Evaluation/Performance Measurement

Recipients are expected to participate in the planning and implementation of program and process evaluation of the longitudinal database in collaboration with CDC and create an evaluation plan by eight months post-award that monitors progress for completion of major requirements of the award. Proposed evaluation plans will be refined in collaboration with CDC after award.

Proposed evaluation plans are expected to

1. assess adherence to obtaining and maintaining appropriate staffing;
2. monitor achievement of proposed number and diversity of participants for access of initial contact information for telephone-administered and in-person assessments;
3. assess adherence to data quality, data confidentiality and security, and data management protocols;

Translation Plan

Recipients are expected to disseminate findings through peer-reviewed journals, presentations at professional conferences, oral and written communication with the FXS population and the organizations that represent them, and through other appropriate mechanisms (e.g., social media, health education channels). Recipients are expected to develop a plan within 12 months post award for completion of priority analyses (including at least 2 peer-reviewed manuscript submissions each year in years 2 through 5) and their dissemination in collaboration with CDC. The plan should describe

- The priority topics for FXS data analyses,

- How findings will be disseminated through various channels with health policymakers and health systems, and
- How data will inform public health actions to improve the health, functioning, and quality of life of individuals with FXS and their families.

OMB/PRA is expected to apply.

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4. Smith, L., Barker, E., Seltzer, M., Abbeduto, L. & Greenberg, J. (2012). Behavioral phenotype of fragile X syndrome in adolescence and adulthood. *American Journal on Intellectual and Developmental Disabilities,* 117(1), 1-17.
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syndrome. *Disability and Health Journal*, *12*(4), 564-573.
13. Eckert, E., Dominick, K., Pedapati, E., Wink, L., Shaffer, R., Andrews, H., et al. (2019). Pharmacologic interventions for irritability, aggression, agitation and self-injurious behavior in fragile X syndrome: an initial cross-sectional analysis. *Journal of Autism and Developmental Disorders*, *49*(11), 4595-4602.
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15. Trans-NIH Fragile X Coordinating Committee. (October, 2019). NIH Strategic Plan for Research on FMR1-Associated Conditions. Available at: https://www.nichd.nih.gov/sites/default/files/2019-11/NIH_ResearchPlan_FMR1_2019.pdf

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.

Estimated Total Funding: $4,000,000

The estimated total funding (direct and indirect) for the entire period of performance for this NOFO is $4,000,000. The estimated total funding (direct and indirect) for Year 1 of this NOFO is $800,000. Awards issued under this NOFO are contingent upon availability of funds and a sufficient number of meritorious applications.

Anticipated Number of Awards: 1

A single award of an estimated $800,000 for year 1 is anticipated if applicants propose recruiting study participants from a group of clinics to achieve the overall study minimum sample size of 600 participants over the entire period of performance. Applicants may alternatively propose to recruit from a single clinic, in which case the award would reflect the proportionate proposed sample size. For example, if an applicant proposes to recruit 360 participants over the period of performance (i.e., 60% of the total sample needed for this study), the award ceiling would be approximately 60% of the total available funding. Five to seven smaller awards of an estimated $150,000 for year 1 are anticipated if applicants propose recruiting a smaller sample from an individual clinic. Because the scope of the proposed research may vary from application to application, it is also anticipated that the size of 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.

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

Award ceiling and floor are for the first 12-month budget period only.

Award Ceiling:	$800,000 Per Budget Period
Award Floor:	$0 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:	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:

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 not include collaborators or consultants from foreign institutions. All applicable federal laws and policies apply.

3. Additional Information on Eligibility

For an application to be considered, the application must be responsive to these Special Eligibility Requirements. If your application is incomplete or non-responsive to the special eligibility requirements listed in this section, it will not enter into the review process.

All applicants must document that they will have access to individual contact information and data from previous FORWARD participants for all clinics they propose to include in their recruitment pool.

Therefore, applicants must either:

1. be the entities that collected the original FORWARD data, and therefore have the information needed to reach these individuals for additional data collection;

OR

2. have established collaborative agreements to work with the entities that originally collected contact information and data from FORWARD participants (i.e., former FORWARD recipients) so that they can reach the FORWARD participants for the data collection as outlined in this NOFO.

4. Justification for Less than Maximum Competition

N/A

5. Responsiveness

If the Responsiveness information requested below is incomplete or non-responsive to these requirements, the application will not enter into the review process.

All applicants must document that they will have access to individual contact information and data from previous FORWARD participants for all clinics they propose to include in their recruitment pool as evidenced by one of the following methods:

1. Applicants must provide evidence (e.g., notice of award for the original FORWARD studies) that their institution was one of the original entities that collected and therefore has this information for previous FORWARD participants

OR

2. Applicants must provide sufficient evidence to show that they will have legal access to the specified data sources for the FORWARD participants they propose to collect data from in this NOFO. A site may collaborate to follow up with FORWARD participants from other sites (in addition to their own) to maximize their sample pool. In this case, evidence such as a subcontract or memorandum of understanding between the relevant entities should be provided in the application. Data needed for the follow-up study includes identifiable contact information to reach FORWARD participants (e.g., addresses, phone numbers, email addresses, etc.) and information confirming consent for follow-up.

Responsiveness elements must be clearly labeled and presented in Appendix A of the application. If the application is incomplete or non-responsive to these requirements, it will not enter the review process.

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://cage.dla.mil/

- 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/index.html .
- 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.

Only one application per institution (normally identified by having a unique DUNS number) is allowed.

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-f/general-forms-f.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.

In conjunction with the SF424 (R&R) components, CDC grant applicants should also complete and submit additional components titled "PHS398." Note the PHS398 should include assurances and certifications, additional data required by the agency for a complete application. While these are not identical to the PHS398 application form pages, the PHS398 reference is used to distinguish these additional data requirements from the data collected in the SF424 (R&R) components. A complete application to CDC will include SF424 (R&R) and PHS398 components. A complete application to CDC will include SF424 (R&R) and PHS398 components. These forms can be downloaded from http://grants.nih.gov/grants/forms.htm

3. Letter of Intent

Due Date for Letter of Intent: **12/07/2020**
Although a letter of intent is not required, is not binding, and does not enter the review of a subsequent application, the information that it contains allows CIO staff to estimate the potential review workload and plan the review.

By the date listed above and in Part 1. Overview Information, prospective applicants are asked to submit a letter of intent that includes the following information:

- Name of the Applicant
- Descriptive title of proposed research
- Name, address, and telephone number of the PD(s)/PI(s)
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity

The letter of intent should be emailed to:

Dionne Godette-Greer, PhD

Scientific Program Official

Extramural Research Program Operations and Services

Centers for Disease Control and Prevention

4770 Buford Highway, NE

Mailstop S107-8

Atlanta, GA 30342

Telephone: (404) 498-3213

Email: qal6@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-f/general-forms-f.pdf and http://grants.nih.gov/grants/how-to-apply-application-guide.htm 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-f/general-forms-f.pdf and here: http://grants.nih.gov/grants/how-to-apply-application-guide.htm 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:
• 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 -
this section should address access to identifiable and de-identified data);
• Statement of the 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 (this section should address archiving and preservation of identifiable and deidentified
data).
Examples of DMPs may be found here: USGS, http://www.usgs.gov/products/data-and-tools/data-management/data-management-plans

Research Plan

Research plans of applicants should address activities that will be conducted over the entire period of performance and should include the following items:

Expertise

Document (with curriculum vitae) and describe experience and expertise in

1. Conducting, presenting, and publishing on FXS research related to cognitive, behavioral, and adaptive skills outcomes, including the ability to produce high-quality outputs (e.g., publications in peer-reviewed journals, presentation at high-profile meetings).
2. Conducting assessments of participants in large-scale research studies and the ability to successfully plan and implement data collection and coordination objectives outlined in

this NOFO, including

- The scope, complexity, and size (including final sample size) of previous studies;
- Age ranges, demographic characteristics including race/ethnicity, and developmental characteristics of the study sample(s);
- Specific developmental areas measured and/or tests used in previous studies,
- Procedures for quality control and quality assurance; and
- Measures of implementation success (e.g., enrollment and completion rates).

Capacity and Approach

Participant Enrollment and Data Collection

Describe capacity and planned approach to the following:

1. Identify and recruit a sufficient number of participants born between 2003 and 2017 (inclusive) to achieve expected sample sizes from each birth cohort, utilizing participants from FORWARD to the extent possible. Applications for the full budget ceiling amount are expected to enroll, assess, and complete data collection (including telephone interviews) for a minimum of 150 individuals with FXS for each of the 4 years of data collection in this NOFO (i.e., 600 individuals over the five-year project period), approximately equally divided among the three birth cohorts. Applications for lower budget amounts are expected to enroll, assess, and complete data collection on a proportionate sample size (e.g., if requesting 60% of the funding ceiling, applicants are expected to enroll, assess, and complete data collection on a minimum of 90 individuals each year), to ensure the overall NOFO aims of at least 150 participants each year, for a minimum of 600 individuals;
2. Obtain informed consent to provide the CDC contractor with contact information of eligible caregivers for the telephone survey;
3. Administer in-person standardized assessments to measure cognitive, behavioral, and other functional outcomes with an appropriate minimum number of participants per year of data collection to meet study sample size goals;
4. Respond to participant inquiries;
5. Document and provide summary information on patients who attend the clinics that participate in the longitudinal database, indicating how many patients were approached for participation, how many patients were not approached, and of those approached how many patients declined participation;
6. Encourage diversity of participants by racial/ethnic groups, socioeconomic status, and other indicators of health disparities that represent their clinic population;
7. Discuss strategies that will be implemented to engage new partners that care for the child and adolescent FXS population and describe how new clinics or other organizations involved with the child and adolescent FXS population will participate;
8. If an applicant is representing multiple clinics, the applicant must have an established, documented relationship with FXS specialty clinics, provide documentation of the relationship with each clinic (e.g., letter of support or memorandum of agreement), and describe how the applicant will interact with the FXS specialty clinics to support the collection of longitudinal data; and
9. Describe the compensation plan, if proposing clinic and participant compensation for

participation in the longitudinal database.

Partnerships and Collaborations

Describe capacity and planned approach to the following:

1. Participate and take on leadership roles in multi-site collaborative research programs;
2. Adhere to standard protocols, data collection, and data management for multi-site collaborative research programs;
3. Maintain confidentiality and privacy of participants;
4. Contribute to a shared pool of de-identified data and common data sharing guidelines for analysis, presentation, publication, data release, and data return; and
5. Obtain and maintain IRB approval and adhere to rules for protection of human subjects.

Management and Staffing

1. Describe a management and staffing plan that includes activities, roles, and responsibilities to
    - Ensure collection of standardized data on participants enrolled in the longitudinal database;
    - Enroll new participants with full-mutation FXS and collect standardized data;
    - Manage communication between sites participating in the longitudinal database, the CDC contractor, CDC, and other relevant stakeholders;
    - Maintain a secure repository for all documents pertaining to the longitudinal database; and
    - Ensure satisfactory participation in the longitudinal database and assist sites with troubleshooting as needed.
2. Provide a clear management and staffing plan to support all data collection activities. Collectively, the PI and co-investigators should demonstrate expertise in epidemiology, developmental disabilities, and statistics, as well as at least one specialty area in child psychiatry, developmental psychology, pediatric medicine, or genetics.
3. If the applicant proposes to include Spanish-speaking participants, describe the resources and staff expertise necessary to conduct the in-person assessments in Spanish.

Budget

Provide a detailed budget and line-item justification of all operating expenses that are consistent with the planned activities of the proposed project, including the following:

- Personnel costs, including salary and travel costs;
- Participant mailings and research participation incentives; and
- Miscellaneous (e.g., materials, such as water and snacks, to ensure participant comfort at the in-person visit).

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 25 pages. Supporting materials for the Research Plan narrative included as appendices may not exceed 10 PDF files with a maximum of 25 pages for all appendices. Pages that exceed page limits described in this NOFO will be removed and not forwarded for peer review, potentially affecting an application's score.

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-f/general-forms-f.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

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," be sure to save time stamped, documented rejection notices, and 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 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: **01/11/2021**

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)

This initiative is not subject to intergovernmental review.

11. Funding Restrictions

Expanded Authority:

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 and speak to your GMS.

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.

Protecting Life in Global Health Assistance:

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/additional-requirements/ar-35.html).

Public Health Data:

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.

Data Management Plan:

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/additional-requirements/ar-25.html for revised AR-25.

Human Subjects:

Funds relating to the conduct of research involving human subjects will be restricted until the appropriate assurances and Institutional Review Board (IRB) approvals are in place. Copies of all current local IRB approval letters and local IRB approved protocols (and CDC IRB approval letters, if applicable) will be required to lift restrictions.

If the proposed research project involves more than one institution and will be conducted in the United States, awardees are expected to use a single Institutional Review Board (sIRB) to conduct the ethical review required by HHS regulations for the Protections of Human Subjects Research, and include a single IRB plan in the application, unless review by a sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy or a compelling justification based on ethical or human subjects protection issues or other well-justified reasons is provided. Exceptions will be reviewed and approved by CDC in accordance with Department of Health and Human Services (DHHS) Regulations (Title 45 Code of Federal Regulations Part 46), or a restriction may be placed on the award. For more information, please contact the scientific/research contact included on this NOFO.
Note: The sIRB requirement applies to participating sites in the United States. Foreign sites participating in CDC-funded, cooperative research studies are not expected to follow the requirement for sIRB.

Funds will be restricted until

- IRB and OMB/PRA (if needed) approvals are obtained. IRB approval letters must be dated and should specify the name of the NOFO or title of the project covered, and the expiration date or lack of need for continuation review. If and when new supplements are added to the protocol, dated IRB approval letters for protocol amendments are required. If the amendment approval letter does not specify the content of the amendment, a summary of the amendment request that was submitted to the IRB is required. Recipient organizations that rely on other institutions for their IRB review responsibilities shall provide documentation of the reliance and the IRB approval. A sample written agreement is available at https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/forms/irb-authorization-agreement/index.html
- Human Subjects Education Requirement documentation is provided for any new key personnel or other significant contributors involved in the design or conduct or research involving human subjects.

Applicants are advised that any activities involving standard information collection (i.e., surveys, questionnaires, data requests, etc.) from 10 or more non-federal individual/entities are subject to Paperwork Reduction Act (PRA) requirements and may require the CDC to coordinate an OMB/PRA approval request.

Reimbursement of pre-award costs is not allowed. All HHS/CDC awards are subject to the terms and conditions, cost principles, 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.

For more information on expanded authority and pre-award costs, go to http://www.hhs.gov/asfr/ogapa/aboutog/hhsgps107.pdf or speak with your Grants Management Specialist (GMS).

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. Upload the questionnaire and supporting documents as an attachment in the "12. Other Attachments" section of the "RESEARCH & RELATED Other Project Information" section of the application. 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 (https://grants.nih.gov/grants/how-to-apply-application-guide.html).

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 (https://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.

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 application document an understanding of the potential impact of this work on the health and well-being of the population living with FXS?
- Does the application document a sufficient understanding of how this work will be influential in the FXS clinical and research communities?
- Does the application document an understanding of how the study could lead to future investigations and/or open new areas of research, and how they could contribute to these future activities?
- Does the application document a sufficient understanding of the importance of communicating the significance of this work to a variety of stakeholders?

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 PI have a record of research and peer-reviewed publications in the field of FXS clinical care and/or public health research?
- Has the applicant demonstrated a track record of collaborating with other FXS specialty clinics?
- Does the applicant have a track record in conducting and analyzing the results of standardized in-person assessments, in particular regarding those involving individuals with developmental disabilities?
- Has the applicant adequately addressed and planned for collaboration with other sites, the CDC contractor, and CDC to discuss study implementation and progress?

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?

- Does the application document an adequate understanding of how this research could improve the care of people affected by FXS?
- Does the application document how the proposed methods build on previous experience with FXS research and provide a high likelihood of success in expanding the understanding of the health and functional outcomes of individuals identified in early childhood with FXS across their lifespan and what factors may improve these outcomes?
- Does the applicant seek to implement innovative participant recruitment and retention methods to maximize recruitment, retention, and diversity of participants?
- Does the applicant propose innovative and diverse data collection methods and capabilities to assess individuals with intellectual disabilities?

Approach

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?

- Has the applicant demonstrated an effective plan to contribute timely and high-quality cognitive, behavioral, and adaptive skill data to the longitudinal database?
- Can the applicant recruit, assess, and complete data collection on a sufficient number of

eligible participants to meet application and/or study sample size goals?

- Has the applicant provided an adequate staffing and resources plan, including a description of staff time commitments and necessary expertise of staff in critical areas of implementation (i.e., clinical supervision and psychometric assessment)?
- Are the partner(s) identified by the applicant adequate to accomplish the goals and objectives? Does the applicant have a sufficient plan to continue engaging partners? Does the applicant have documented support from the partner(s)?
- Has the applicant described procedures to maximize retention and participation, including active follow-up of families who were scheduled for an in-person visit but did not complete the visit for any reason, and strategies to reach and retain participants of diverse demographic characteristics, including race/ethnicity?
- If the applicant proposes to include Spanish-speaking participants, are there resources and staff with expertise necessary to conduct the research in other languages?
- Has the applicant demonstrated willingness to conduct quality control activities for standardized assessments?
- Has the applicant outlined data confidentiality and security procedures, including storage of psychometric assessment test results?

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?

- Does the applicant's proposed sampling plan represent the racial/ethnic composition of the clinic population?
- Has the applicant provided evidence for access to clinical space to reasonably accommodate participants?
- Does the proposed clinic space have adequate security, privacy, accessibility, furniture, and lighting?
- Has the applicant demonstrated the ability and intent to collaborate with multiple FXS specialty clinics to achieve the objectives of this NOFO?
- Does the project utilize critical partnerships or collaborations? Does the project support key stakeholder involvement throughout the research process? Has the applicant demonstrated support from partners identified in the approach and research plans?

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 four 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) 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 4) 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://olaw.nih.gov/guidance/vertebrate-animal-section.htm).

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.

Data Management Plan (DMP)

CDC requires awardees for projects that involve the collection or generation of public health data with federal funds to submit a Data Management Plan (DMP) prior to the initiation of generating or collecting public health data unless CDC will aggregate and disseminate the data. Public health data means digitally recorded factual material commonly accepted in the scientific community as a basis for public health findings, conclusions, and implementation. In initial funding applications, the DMP should be addressed within the Resource Sharing Plan section of the PHS 398 Research Plan Component of the application, either as a stand-alone DMP within this section or with a statement explaining why a DMP is not included. The DMP must be updated and submitted to CDC at least annually, or whenever plans for data collection or generation activities change. Costs associated with developing and implementing a DMP, including costs of sharing, archiving and long-term preservation, may be included in the budget submissions for grants and cooperative agreements. The contents of the DMP are described in AR-25. Visit link https://www.cdc.gov/chronicdisease/programs-impact/nofo/index.htm for OMB approved template and guidance.

Public health data are expected to be made freely available to the public (in a de-identified format) and archived long-term unless there are compelling reasons not to do so. When it is not feasible to make data freely available to the public, it may be possible to make data available to users on a restricted basis. The DMP should describe the expected level of public access, if any, and must justify the planned access level and describe how privacy and confidentiality will be protected. The final version of a collected and/or generated data set intended for release or sharing should be made available within thirty (30) months after the end of the data collection or generation, except surveillance data from ongoing surveillance systems which should be made accessible within 12 months of the end of a collection cycle. Awardees who fail to release public health data in a timely fashion may be subject to procedures normally used to address lack of compliance consistent with applicable authorities, regulations, policies or terms of their award. For data underlying scientific publications such as peer review journal articles, awardee should make the data available coincident with publication of the paper, unless the data set is already available via a release or sharing mechanism. At a minimum, release of the data set accompanying a scientific paper should consist of a machine-readable version of the data tables shown in the paper.

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:

- 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 - this section should address access to identifiable and de-identified data);
- Statement of the 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 (this section should address archiving and preservation of identifiable and de-identified data).

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:

- Will undergo a selection process in which all responsive applications will be discussed and assigned an overall impact/priority score.

- 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 recommendations:

- 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.

- Study population size
- Geographic distribution of clinics
- Racial and ethnic diversity of the study population

Review of risk posed by applicants.

Prior to making a Federal award, CDC is required by 31 U.S.C. 3321 and 41 U.S.C. 2313 to review information available through any OMB-designated repositories of government-wide eligibility qualification or financial integrity information as appropriate. See also suspension and debarment requirements at 2 CFR parts 180 and 376.

In accordance 41 U.S.C. 2313, CDC is required to review the non-public segment of the OMB-designated integrity and performance system accessible through SAM (currently the Federal Recipient Performance and Integrity Information System (FAPIIS)) prior to making a Federal award where the Federal share is expected to exceed the simplified acquisition threshold, defined in 41 U.S.C. 134, over the period of performance. At a minimum, the information in the system for a prior Federal award recipient must demonstrate a satisfactory record of executing programs or activities under Federal grants, cooperative agreements, or procurement awards; and integrity and business ethics. CDC may make a Federal award to a recipient who does not fully meet these standards, if it is determined that the information is not relevant to the current Federal award under consideration or there are specific conditions that can appropriately mitigate the effects of the non-Federal entity's risk in accordance with 45 CFR §75.207.

CDC’s framework for evaluating the risks posed by an applicant may incorporate results of the evaluation of the applicant's eligibility or the quality of its application. If it is determined that a Federal award will be made, special conditions that correspond to the degree of risk assessed may be applied to the Federal award. The evaluation criteria is described in this Notice of Funding Opportunity.

In evaluating risks posed by applicants, CDC will use a risk-based approach and may consider any items such as the following:

(1) Financial stability;
(2) Quality of management systems and ability to meet the management standards prescribed in this part;
(3) History of performance. The applicant's record in managing Federal awards, if it is a prior recipient of Federal awards, including timeliness of compliance with applicable reporting requirements, conformance to the terms and conditions of previous Federal awards, and if applicable, the extent to which any previously awarded amounts will be expended prior to future awards;
(4) Reports and findings from audits performed under subpart F 45 CFR 75 or the reports and findings of any other available audits; and
(5) The applicant's ability to effectively implement statutory, regulatory, or other requirements imposed on non-Federal entities.

CDC must comply with the guidelines on government-wide suspension and debarment in 2 CFR part 180, and require non-Federal entities to comply with these provisions. These provisions restrict Federal awards, subawards and contracts with certain parties that are debarred, suspended or otherwise excluded from or ineligible for participation in Federal programs or activities.

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: https://www.archives.gov/federal-register/cfr.

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-3: Animal Subjects Requirements

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-17: Peer and Technical Reviews of Final Reports of Health Studies – ATSDR

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

ARs applicable to Conference Awards:

AR-20: Conference Support

AR-27: Conference Disclaimer and Use of Logos

Organization Specific ARs:

AR-8: Public Health System Reporting Requirements

AR-15: Proof of Non-profit Status

AR 23: Compliance with 45 C.F.R. Part 87

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/additional-requirements/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/additional-requirements/ar-36.html.

4. Cooperative Agreement Terms and Conditions

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Part 75, and other HHS, PHS, and CDC grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial CDC programmatic involvement with the recipients is anticipated during the performance of the activities. Under the cooperative agreement, the HHS/CDC purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; CDC Project Officers are not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the recipients for the project as a whole, although specific tasks and activities may be shared among the recipients and HHS/CDC as defined below.

The PD(s)/PI(s) will have the primary responsibility for the following:

- Complying with the responsibilities for the Extramural Investigators as described in the Policy on Public Health Research and Nonresearch Data Management and Access **https://www.cdc.gov/grants/additionalrequirements/ar-25.html** ;
- Maintaining an adequate management and staffing plan to support all project activities.
- Oversight of project management and all scientific aspects of the project at their site(s) and for the study overall in collaboration with CDC, a CDC survey and data center contractor, and other FXS and SEED recipients
- Obtaining and maintaining appropriate institutional review board approval for all institutions or individuals participating in research involving human subjects, providing certification for any new key personnel or other significant contributors involved in the

design or conduct of research involving human subjects that they have completed an educational program in the protection of human subjects.
- Working collaboratively with CDC, a CDC survey and data center contractor, and other FXS and SEED recipients on all aspects of protocol development, study implementation, data collection, and study conduct.
- Actively participating in meetings, webinars, workgroup meetings, and conference calls. Ensuring timely responses to all Quality Assurance/Quality Control (QA/QC) activities and requests.
- Adherence to established Publication and Data Sharing Guidelines. These guidelines include CDC specific scientific requirements pertaining to CDC clearance.
- Providing accurate and timely reports, per guidance in the "Reporting" section

CDC staff have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- Assisting the PI, as needed, in complying with the Investigator responsibilities described in the Policy on Public Health Research and Nonresearch Data Management and Access https://www.cdc.gov/grants/additionalrequirements/ar-25.html
- Provide management and oversight of the award.
- Provide scientific consultation as requested by recipients.
- Support recipients' activities by consulting and providing scientific and public health consultation and assistance in the development of activities related to the cooperative agreement.
- Assist in facilitating communication among recipients for the development of common multi-center protocol(s), quality control, interim data monitoring, data analyses, interpretation, reporting and coordination.
- Ensure adherence of human subject requirements and approval of study protocol by IRB and OMB, for all cooperating institutions participating in the study.
- Facilitate the process of obtaining Certificates of Confidentiality in the form of 301(d), if appropriate.
- Collaborate to produce and co-author technical reports and manuscripts for peer-reviewed publications as appropriate. Aid with joint analysis with aggregate data.

Recipients will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and CDC policies.

- Additionally, an agency program official or CIO program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. The Project Officer will be:
    - Named in the Notice of Grant Award (NGA) as the Program Official to provide oversight and assure overall scientific and programmatic stewardship of the award;
    - Monitor performance against approved project objectives; and
    - Ensure assessment of the public health impact of the research conducted under

this funding opportunity announcement and promote translation of promising practices, programs, interventions, and other results from the research.

Areas of Joint Responsibility include:

- Develop the final protocol for the follow-up study assessment;
- Discuss any difficulties in implementing the methodology for the study;
- Identify how to reconcile differences in approaches to the study;
- Identify and recommend solutions to unexpected study problems; and
- Discuss ways to efficiently coordinate study activities and best practices.

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).

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 the Payment Management System (PMS) **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:

N/A

2. Annual Federal Financial Reporting The Annual Federal Financial Report (FFR) SF 425 is required and must be submitted through the Payment Management System (PMS) 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 is 120 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 on the Payment Management System (PMS) can be found at https://pms.psc.gov.
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://era.nih.gov/ 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, health care 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

Scientific/Research Contact(s)

Dionne Godette-Greer, PhD

Scientific Program Official

Extramural Research Program Operations and Services

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Email: qal6@cdc.gov

Peer Review Contact(s)

Jaya Raman, PhD

Scientific Review Official

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Telephone: (770) 488-6511

Email: kva5@cdc.gov

Financial/Grants Management Contact(s)

Cynthia Thompson

Centers for Disease Control and Prevention

Office of Grants Services

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Email: cbt1@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.

Sections 301 and 317C of the Public Health Service Act, (42 USC Sections 241 and 247b-4), as amended.