

Centers for Disease Control and Prevention

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

Using Longitudinal Data to Characterize The Natural History of Fragile X Syndrome to Improve Service

RFA-DD-15-003

Application Due Date: 02/20/2020

Using Longitudinal Data to Characterize The Natural History of Fragile X Syndrome to Improve Service

RFA-DD-15-003

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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 Extramural Research Program Office (NCBDDD ERPO)
National Center on Birth Defects and Developmental Disabilities (NCBDDD)

Funding Opportunity Announcement (FOA) Title

Using Longitudinal Data to Characterize The Natural History of Fragile X Syndrome to Improve Service

Activity Code

Amendment 2 - made on December 30, 2019.

This supplemental funding opportunity will provide FY20 funds to existing recipients to maximize the value of activities undertaken in accordance with CDC-RFA-DD-15-003, the activities supported with this supplemental funding will extend the project period for Component A and B for one additional year.

See Section VIII. Other Information -Appendix A

AMENDMENT 1 made on February 10, 015.

U01

Funding Opportunity Announcement Type

Reissue of CDC-RFA-DD-15-003

Funding Opportunity Announcement Number

RFA-DD-15-003

Catalog of Federal Domestic Assistance (CFDA) Number(s)

93.315

Category of Funding Activity:

Health

FOA Purpose

The purpose of this FOA is to contribute to the understanding of the natural history of fragile X syndrome (FXS) across the lifespan, explore effective strategies to increase participation in the longitudinal database for minority, underserved, and adults living with FXS, and test approaches to measure cognitive and behavioral function in the FXS population.

Component A

The purpose of Component A is to coordinate and expand the FORWARD longitudinal database to describe the natural history of FXS across the life span and characterize the impact of interventions and treatments on both health outcomes and quality of life.

Component B

The purpose of Component B is to support a Data Coordinating Center to manage the receipt, processing, and analysis of patient, caregiver, clinician, and laboratory reported data from clinics participating in the longitudinal database and other data sources.

Component C

The purposes of Component C are to enhance participation in the longitudinal database; develop, implement, and evaluate a plan to increase participation of minority and underserved populations in the longitudinal database; and test approaches to measure cognitive and behavioral function in the FXS population.

Key Dates

Publication Date:	**To receive notification of any changes to RFA-DD-15-003, 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:	**01/29/2020**
Application Due Date:	**02/20/2020**

On-time submission requires that electronic applications be error-free and made available to CDC for processing from eRA Commons on or before the deadline date. Applications must be submitted to and validated successfully by Grants.gov/eRA Commons no later than 5:00 PM U.S. Eastern Time. Note: HHS/CDC grant submission procedures do not provide a period of time beyond the application due date 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:	**04/06/2020**

The 04/06/2020 date listed above is an approximate date for this supplemental funding opportunity.

Secondary Review:	**04/06/2020**
Estimated Start Date:	**09/01/2020**

Estimated Start Date for this supplemental funding opportunity: September 1, 2020.

Expiration Date:	**02/21/2020**
Due Dates for E.O. 12372:	**Executive Order 12372 does not apply to this program.**

Required Application Instructions

It is critical that applicants follow the instructions in the SF 424 (R&R) Application Guide

except where instructed to do otherwise in this FOA. Conformance to all requirements (both in the Application Guide and the FOA) 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.

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

Executive Summary

- **Purpose.** The purpose of this FOA is to contribute to the understanding of the natural history of fragile X syndrome (FXS) across the lifespan, explore effective strategies to increase participation in the longitudinal database for minority, underserved, and adults living with FXS, and test approaches to measure cognitive and behavioral function in the FXS population.
- **Mechanism of Support.** This funding opportunity will use the cooperative agreement funding mechanism (CDC U-01).
- **Funds Available and Anticipated Number of Awards.** Component A: Total funding is expected to be $1,750,000 (direct and indirect) over the five year project period ($350,000/year). It is anticipated that 1 award will be made to a single recipient for up to $350,000 in FY 2015. Component B: Total funding is expected to be $1,000,000 (direct and indirect) over the five year project period ($200,000/year). It is anticipated that 1 award of up to $200,000 will be made in FY 2015. Component C: Total funding is expected to be $1,500,000 (direct and indirect) over the five year project ($300,000/year). It is anticipated that up to 3 awards of up to $100,000 each will be made in FY 2015.
- **Budget and Project Period.** Component A: The estimated total funding (direct and indirect) for the first year (12 month budget period from September 1, 2015 to August 31, 2016) will be up to $350,000. The total funding available for the project period will be approximately $1,750,000. The project period will run from September 1, 2015 to August 31, 2020. Component B: The estimated total funding (direct and indirect) for the first year (12 month budget period from September 1, 2015 to August 31, 2016) will be up to $200,000. The total funding available for the project period will be approximately $1,000,000. The project period will run from September 1, 2015 to August 31, 2020. Component C: The estimated total funding (direct and indirect) for the first year (12 month budget period from September 1, 2015 to August 31, 2016) will be up to $300,000. The total funding available for the project period will be approximately $1,500,000. The project period for Components A, B and C will run from September 1, 2015 to August 31, 2020.
- **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 must designate a PI. Applications may designate co-PIs, however, the first PI listed will be the designated PI and official "contact PI" for all correspondence.
- **Number of Applications.** Only one application per institution (normally identified by having a unique DUNS number) per component is allowed. Applicants can apply for more than one component. If applying for more than one component, a separate application for each component is required.
- **Application Type.** New (type 1)
- **Special Date(s).** CDC will conduct one conference call for prospective applicants. This session will provide information about the FOA and will answer questions pertinent to preparing applications in response to this FOA.
    - Conference Call Details:
    - Date: January 15, 2015 from 1:00 - 2:00 pm (EST)
    - Call-in Number: 1-855-644-0229Toll Free
    - Participant Pass Code: 7457938
- **Application Materials.** See Section IV.1 for application materials.
- **Hearing Impaired.** Telecommunications for the hearing impaired are available at: TTY: (770) 488-2783.

Part 2. Full Text

Section I. Funding Opportunity Description

Statutory Authority

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

1. Background and Purpose

Fragile X syndrome (FXS) is the most common known inherited cause of intellectual disability (ID). FXS affects both males and females. However, females can have milder symptoms than males. The exact number of people who have FXS is unknown, but it has been estimated that about 1 in 4,000 - 5,000 males and about 1 in 6,000 – 8,000 females are born with the disorder. People who have FXS show a range of intellectual disability and may also experience emotional, behavioral, sensory, and/or social difficulties.

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 fragile X

mental retardation 1 (FMR1) gene. However, we are just beginning to understand how this complex condition affects individuals and their families. Some parents spend years taking their child to different doctors before getting a diagnosis of FXS. After the diagnosis, they still may struggle with the behavioral and communication challenges or co-occurring conditions that can come with FXS. The more we know about this population across the lifespan, both from a clinical perspective and a parent/caregiver perspective, the better we can design services and care that will improve the lives of those affected.

To date, limited data are available to describe the prevalence of co-occurring conditions in the FXS population (such as Autism, ADHD, anxiety, depression, and seizures) and the spectrum of interventions used to treat symptoms. Data are limited with regard to determining if these interventions improve short-or long-term health and wellness outcomes among people with fragile X syndrome. Further, research aimed at understanding unmet needs and challenges faced by individuals who have FXS could also benefit the broader population of individuals living with intellectual and developmental disabilities. CDC has funded two pilot studies to determine the feasibility of collecting data needed to expand our understanding of FXS.

The first pilot study (2008-2011) tested the infrastructure required to carry out multi-site research in FXS. Results of this study demonstrated that working with The Fragile X Clinical and Research Consortium (FXCRC) was an effective way to reach clinics and demonstrated that facilitated research across multiple FXS specialty clinics could be successfully conducted. The second pilot study (2011-2015) is currently testing the ability of this infrastructure to collect and manage longitudinal data. FXCRC launched the Fragile X Online Registry With Accessible Research Database (FORWARD), and is working with FXS specialty clinics across the country to contribute data on individuals diagnosed with FXS, ages 0-24 years of age. The FORWARD Database has thus far demonstrated that longitudinal data can be successfully collected on participants.

The next FOA will build on this work by expanding it in two ways: 1) collecting additional longitudinal data on participants already enrolled, and 2) enrolling new participants with a focus on minority and underserved populations and the adult FXS population (>24 years of age). The expansion of the longitudinal database will provide a data resource that clinicians and researchers can use to address clinical care and public health research questions. This could include questions such as: what are the most common co-occurring conditions across the life span? How often do they occur in the FXS population? What types of interventions and treatments are used to address symptomology? What are the service needs of the adult fragile X population?

In May 2014, CDC gathered FXS stakeholders to discuss gaps in public health knowledge about FXS, identified through a structured literature review. Working from a summary of the latest FXS scientific literature, CDC identified six topic areas where public health research and programs can contribute knowledge about this complex condition: 1) epidemiology, 2) early identification and screening, 3) impact on individuals and families, 4) FXS across the lifespan, 5) co-occurring conditions, and 6) interventions and outcome measures. Researchers, clinicians, behavior and education specialists, patient advocates, and families had an opportunity to discuss challenges and strategies for addressing gaps in each of these six areas. This FOA will address gaps identified through this process in five of the six topic areas.

This FOA will support the epidemiologic collection of data that will support a more robust and

inclusive description of the FXS population (e.g. gender, age, race, ethnicity, and socio-economic factors). With regard to impact on individuals and families, this FOA supports the continued collection of longitudinal data that can provide a data resource for answering research questions related to how FXS is impacting individuals and families. In relation to topics 4 and 5 listed above, it is imperative to think about the transitions individuals living with FXS navigate throughout their lifespan. Little is known about the health and social issues adults with FXS face and there are very limited data on aging with FXS. Work undertaken through this FOA can begin to shed light on the transition out of school, employment issues, daily living and functional skills of adults living with FXS, and guardianship of adults living with FXS. The research supported by this FOA can further describe conditions that occur more frequently in FXS patients (e.g., anxiety, ADHD, seizures, depression, and autism) and provide insight into the issues that come with these co-occurring conditions. Testing different ways to measure cognitive or behavioral function and assessing applicability to the FXS population will also result from work undertaken as part of this FOA.

The intent of this FOA is to support research that will contribute to: a more robust description of the FXS population, an informed understanding of the natural history of FXS across the lifespan, the impact of treatments and interventions on health outcomes and quality of life, approaches to measuring cognitive and behavioral status in FXS patients, and assessing the impact of treatments and interventions. This FOA builds upon knowledge gleaned through the two pilot studies and uses the lessons learned to collect important longitudinal data that allows for continued public health research in the FXS population. Analyses could generate information to guide parents and health professionals to the best services and outcomes possible, as well as inspire future research aimed at furthering improvements in health and wellness. To achieve this, longitudinal data needs to be collected on individuals already enrolled in the database and new enrollees, in particular adults living with FXS and participants from diverse backgrounds.

To accomplish the intent of the FOA, there are three separate components:

Component A – Coordination of the Longitudinal Database

The purpose of Component A is to coordinate efforts to expand the FORWARD longitudinal database in order to describe the natural history of FXS across the life span and characterize the impact of interventions and treatments on both health outcomes and quality of life.

Component A will expand on the FORWARD longitudinal database in two ways: 1) collect additional data points on individuals already enrolled and 2) enroll new study participants, with a focus on minority and underserved populations and the adult fragile X population (> 24 years of age). New questions directed at the adult FXS population will be developed and piloted.

Component B – Data Coordinating Center

The purpose of Component B is to support a Data Coordinating Center to manage the receipt, processing, and analysis of patient, parent, clinician, and laboratory reported data from clinics participating in the longitudinal database and other sources.

Component C – Enhanced Participation of Fragile X Specialty Clinics

The purpose of Component C is to enhance participation in the longitudinal database; develop, implement, and evaluate a plan to increase participation of minority and underserved

populations in the longitudinal database; and test approaches to measure changes in cognitive function or behavior.

Applicants can apply for more than one component. If applying for more than one component, a separate application for each component must be submitted.

Healthy People 2020 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 2020" and to measuring program performance as stipulated by the Government Performance and Review Act (GPRA). This FOA addresses Healthy People 2020 Goal: Improve health-related quality of life and well-being for all individuals.

This FOA will contribute to this Healthy People 2020 goal with regard to the FXS population. Collecting and analyzing longitudinal data can assist researchers and clinicians in answering clinical care and public health research questions. This can facilitate the identification of important therapeutic, behavioral and educational interventions and provide essential information to assist health care and allied professionals in providing better care, with the long-term goal of improving health outcomes and quality of life across the lifespan.

Public Health Impact

FXS is a lifelong condition and in order to address the long-term goal of improving health outcomes and quality of life, gaps in knowledge about the health status of people living with FXS and interventions that may or may not be effective need to be filled. Little is currently known about which interventions and treatments yield the best outcomes. To date, research efforts have primarily focused on children, therefore not much is known about the health status and social wellbeing of adults living with FXS - where they seek specialized care, how aging influences what services are used and needed, and whether caregiver and guardianship challenges change. In addition to collecting longitudinal data on individuals 24 years of age or younger, this project will begin to collect data on individuals over 24 years of age as well. This can provide a much needed epidemiologic profile of the adult FXS population for the first time, leading to interventions and services that can then be developed. Additionally, efforts to include minority and underserved populations will create a more inclusive description of the FXS clinic-based population and provide preliminary data that can be used to investigate if there are differences between subgroups of the population that may be related to health disparities.

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Relevant Work

This work will build on two pilot studies. The first pilot study (2008-2011) tested the infrastructure required to carry out multi-site research in FXS; the Fragile X Clinical and Research Consortium (FXCRC) successfully facilitated research across multiple FXS specialty clinics. The second pilot study (2011-2015) is testing whether it is feasible and effective to

collect and manage longitudinal data. During the second pilot study, the grantee has worked with FXS specialty clinics across the country, in collaboration with the FXCRC, to contribute data on individuals diagnosed with FXS ages 0-24 years of age. Data are currently being collected through the Fragile X Online Registry With Accessible Research Database (FORWARD). Data for the Registry and Database are provided by 24 participating clinics, each with IRB approval, using structured clinician and parent-report forms and standardized parent-report instruments on behavior and communication (i.e. SRS, SCQ, ABC-C). More information can be found at www.fxcrc.org.

2. Approach

This work should build on previous efforts to develop and implement the FORWARD Registry and Database as well as address gaps in knowledge identified by a structured literature review and input from stakeholders and FXS experts. This FOA will support expansion of the FORWARD database to include adults living with FXS and encourage participation of underserved and minority populations. To address the need to understand more about the adult FXS population the approach shall include, but is not limited to, developing and piloting the collection of variables specific to adult individuals living with FXS (e.g. clinical, occupational, familial, and social service needs, as well as guardianship and caregiver issues).

This FOA is comprised of three separate components aimed at collecting and analyzing data that can provide a robust description of the FXS population, an informed understanding of the natural history of FXS across the lifespan, an analysis of the impact of treatments and interventions on health outcomes and quality of life, and improved approaches to measuring cognitive and behavioral status in FXS patients.

Objectives/Outcomes

Component A – Coordination of the Longitudinal Database: Outcomes

Component A will utilize a national coordinator to support and coordinate data collection activities across fragile X specialty clinics and facilitate the expansion of the longitudinal database to include adults living with FXS. The national coordinator may collaborate with the Fragile X Clinical Research Consortium (FXCRC) to facilitate access to study participants from the specialty clinics. The national coordinator will collaborate with the Data Coordinating Center to ensure timely and accurate data collection.

Component A – Coordination of the Longitudinal Database: Objectives

- Using the data collection tools of the FORWARD Registry and Database, expand on longitudinal data by collecting four additional data points on at least 150 individuals with fragile X syndrome already enrolled in the longitudinal database; three additional data points on at least 175 enrollees; and two additional data points on at least 225 enrollees; and enroll at least 450 new participants (all ages) with fragile X syndrome into the database.
- Develop and pilot questions to obtain new data specific to the adult FXS population – clinical and social services used and needed across the lifespan as well as possible occupational, familial, sociocultural, and guardianship factors that need to be addressed along with other caregiver needs.
- Collaborate with clinicians and researchers from the sites participating in the longitudinal database, the PIs of Components B and C, and CDC representatives to identify important clinical care and public health research questions and utilize data from the longitudinal database to address them.
- Collaborate with the PIs of Components B and C and CDC representatives to establish and implement guidelines and processes for data analysis and publications.
- Participate in a Steering Committee that is intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site from Components A, B, and C and CDC staff. The Steering Committee may consider adding non-voting liaisons from patient oriented organizations, including but not limited to, the National Fragile X Foundation and FRAXA Research Foundation. Addition of non-voting members must be unanimously approved by the designated Steering Committee members described above.
- Develop a sustainability plan for the maintenance and support of the longitudinal database beyond the completion of this FOA.

Component B – Data Coordinating Center: Outcomes

Component B will utilize a Data Coordinating Center to build on the existing longitudinal database to maintain and manage data collected by participating clinics.

Component B – Data Coordinating Center: Objectives

- Build on the existing longitudinal database to provide a data management and analysis center for receipt, processing, and analysis of patient, parent, clinician, and laboratory reported data from the participating clinics or other data sources.
- Conduct ongoing quality control/quality assurance to maintain high quality data
- Create at least one, but no more than two, clean de-identified datasets each year to be used for analysis.
- Issue a “data dictionary” or “documentation of data” to accompany each dataset.
- Collaborate with the PI of Components A and C and CDC representatives to establish and implement guidelines and processes for data analysis and publications.
- Work with clinicians and researchers participating in the longitudinal database to conduct analyses and publish findings.

- Participate in a Steering Committee that is intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site from Components A, B, and C and CDC staff. The Steering Committee may consider adding non-voting liaisons from patient oriented organizations, including but not limited to, the National Fragile X Foundation and FRAXA Research Foundation. Addition of non-voting members must be unanimously approved by the designated Steering Committee members described above.
- Collaborate with clinicians and researchers to conduct analyses using established cleaned datasets.

Component C – Enhanced Participation of Fragile X Specialty Clinics: Outcomes

Component C will engage FXS specialty clinics in the data collection process for the longitudinal database. These clinics will collaborate with the CDC to develop, implement, and evaluate a plan to increase the participation of minority and underserved populations in the longitudinal database and share the results with other fragile X specialty clinics; this may be done by collaborating with the FXCRC. The clinics will use data collected on participants in the longitudinal database to test different ways to measure cognitive and behavioral function and assess if these measures can be used to measure changes in cognitive or behavioral function in this population.

Component C – Enhanced Participation of Fragile X Specialty Clinics: Objectives

- Participate in the longitudinal database – proactively approach at least 85% of currently enrolled participants for follow-up data and approach at least 85% of those not enrolled (all ages) to obtain complete baseline data. This shall include, but is not limited to, developing and implementing a system to track patient participation in FORWARD, identifying patients that have not been offered participation in FORWARD and offering participation at their next visit, documenting patients that have declined participation, alerting clinic staff when enrolled participants are eligible for annual follow-up data, and notifying participants they are due for collection of follow-up data.
- Select approach for enhanced participation and/or enhanced measurement – choose one or both.
    - Enhanced participation (minority and underserved populations)
        - Increase participation in the longitudinal database among minority and underrepresented populations and measure the increases in recruitment and enrollment among these populations.

AND/OR

- Enhanced measurement (outcome measures)
    - Identify and test the reliability, validity, and utility of one or more selected cognitive or behavior measures.
    - Implement the selected measure(s) at least annually for five years and if applicable, compare the performance with one of the standardized parent-report instruments on behavior and communication currently being collected as part of

the FORWARD database: SRS, SCQ, ABC-C.

- Collaborate with the recipients of Components A and B to develop and implement an analysis plan for utilizing data from the longitudinal database.
    - Address clinical care and public health research questions. Examples include a description of the FXS population and subgroups of the population, identifying risk factors for co-occurring conditions, describing interventions and treatments being used and the impact on health and wellness outcomes.
    - Examine approaches selected to enhance participation and/or measurement. Upon completion of enhancement activities, explore stratified analysis by race/ethnicity/socio-demographics or utilize the piloted outcome measure in an analysis.
- Participate in a Steering Committee that is intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site from Components A, B, and C and CDC staff. The Steering Committee may consider adding non-voting liaisons from patient oriented organizations, including but not limited to, the National Fragile X Foundation and FRAXA Research Foundation. Addition of non-voting members must be unanimously approved by the designated Steering Committee members described above.

Target Population

The target populations for this FOA are individuals diagnosed with fragile X syndrome, all ages, currently attending a fragile X specialty clinic and those not attending a FXS specialty clinic but who meet the criteria to be attending; fragile X specialty clinics; other clinics that see FXS cases; and fragile X clinicians and researchers. For Component C, the specific target population is fragile X specialty clinics with an annual expected patient base of at least 30 individuals with full mutation fragile X syndrome of all ages, with an emphasis on individuals with FXS from minority and underserved populations.

Collaboration/Partnerships

Recipients of each of the components are expected to collaborate with one another, the fragile X specialty clinics (this may include collaboration with the Fragile X Clinical and Research Consortium), and the CDC to accomplish the study goals and objectives. The awardee of Component A will be expected to also collaborate with fragile X organizations such as, but not limited to, The National Fragile X Foundation and FRAXA Research Foundation.

Evaluation/Performance Measurement

Recipients of Components A and B are expected to participate in the planning and implementation of Program and Process Evaluation of the longitudinal database in collaboration with CDC. Recipients of Component C, depending on the area of focus, are expected to participate in the planning and implementation of evaluating the utility of identified measures for use in individuals living with FXS or evaluating recruitment strategies targeted at minority and underserved populations.

Translation Plan

Applicants are expected to disseminate findings through peer-reviewed journals, presentations at professional conferences, oral and written communication with the FXS population, and other mechanisms.

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:

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

Estimated Total Funding: $550,000

The estimated total funding for Components A, B, and C of this FOA is expected to be up to $4,250,000 (direct and indirect) over a five year project period.

Component A: Total funding is expected to be up to $1,750,000 (direct and indirect) over the five year project period ($350,000/year). It is anticipated that 1 award will be made to a single recipient for up to $350,000 in FY 2015.

Component B: Total funding is expected to be up to $1,000,000 (direct and indirect) over the five year project period ($200,000/year). It is anticipated that 1 award of up to $200,000 will be made in FY 2015.

Component C: Total funding is expected to be up to $1,500,000 (direct and indirect) over the five year project ($300,000/year). It is anticipated that up to three awards up to $100,000 each will be made in FY 2015.

Awards issued under this FOA are contingent on the availability of funds and submission of a

sufficient number of meritorious applications.

Anticipated Number of Awards: 2

The ceiling of the award for Component A will be $350,000 (including direct and indirect costs). This ceiling is for the first 12-month project period. The range of funding is $0 - $350,000.

The ceiling of the award for Component B will be $200,000 (including direct and indirect costs). This ceiling is for the first 12-month project period. The range of funding is $0 - $200,000.

The ceiling of the award for Component C will be $100,000 (including direct and indirect costs). This ceiling is for the first 12-month project period. The range of funding for up to three awards is $0 - $100,000.

Applications with budget requests greater than the ceiling will be considered non-responsive and will not be reviewed.

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

Award Ceiling: $350,000 Per Project Period

Award Floor: $0 Per Project Period

Total Project Period Length: 1 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 (https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf) will apply to the applications submitted and awards made in response to this NOFO.

Section III. Eligibility Information

1. Eligible Applicants

Eligibility Category:

State governments
County governments
City or township governments
Special district governments
Independent school districts
Public and State controlled institutions of higher education
Native American tribal governments (Federally recognized)

Public housing authorities/Indian housing authorities
Native American tribal organizations (other than Federally recognized tribal governments)
Nonprofits having a 501(c)(3) status with the IRS, other than institutions of higher education
Nonprofits without 501(c)(3) status with the IRS, other than institutions of higher education
Private institutions of higher education
For profit organizations other than small businesses
Small businesses

Additional Eligibility Category:

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

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

Nonprofits Other Than Institutions of Higher Education:

Nonprofits (Other than Institutions of Higher Education)

Governments:

Eligible Agencies of the Federal Government
U.S. Territory or Possession

Other:

Native American tribal organizations (other than Federally recognized tribal governments)

Faith-based or Community-based Organizations
Regional Organizations
Bona Fide Agents: a Bona Fide Agent is an agency/organization identified by the state as eligible to submit an application under the state eligibility in lieu of a state application. If applying as a bona fide agent of a state or local government, a legal, binding agreement from the state or local government as documentation of the status is required. Attach with "Other Attachment Forms" when submitting via www.grants.gov.

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. 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.

4. Justification for Less than Maximum Competition

Not applicable

5. Responsiveness

To be considered responsive to this announcement, applicants may not request funding above the ceiling amount of $350,000 for Component A, $200,000 for Component B, or $100,000 for Component C for Year 1 (includes both direct and indirect costs).

Component C

Applicants must provide a table or figure with 1) the number and basic demographic information (age, gender, race, ethnicity) for the FXS patients seen in the clinic for the past three years, demonstrating greater than or equal to 30 fragile X syndrome patients (all ages) per year; and 2) an estimate of the number of FXS patients the clinic expects to serve each year

between 2015 ? 2020.

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

Applicants should present this responsiveness information for Component C in Appendix A of their application. Incomplete applications, applications submitted after 5:00 PM on the listed application due date or non-responsive applications with budgets that exceed the ceiling of the award will not be entered into 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://eportal.nspa.nato.int/AC135Public/Docs/US%20Instructions%2 0for%20NSPA%20NCAGE.pdf
- System for Award Management (**SAM**) – must maintain current registration in SAM (the replacement system for the Central Contractor Registration) to be renewed annually, https://www.sam.gov/portal/SAM/#1.
- 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 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 registration process at least four (4) weeks prior to the application due date.

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/ asfr/ ogapa/ aboutog/ 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.

Section IV. Application and Submission Information

1. Address to Request Application Package

Applicants must download the SF424 (R&R) application package associated with this funding opportunity from www.Grants.gov.
If access to the Internet is not available or if the applicant encounters difficulty accessing the

forms on-line, contact the HHS/CDC Office of Grants Services (OGS) Technical Information Management Section (TIMS) staff at (770) 488-2700 or ogstims@cdc.gov for further instructions. Hours: Monday - Friday, 7am – 4:30pm U.S. Eastern Time. CDC Telecommunications for the hearing impaired or disabled is available at: TTY 1-888-232-6348.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the SF424 (R&R) Application Guide (http://grants.nih.gov/grants/funding/ 424/SF424_RR_Guide_General_VerC.pdf), except where instructed in this Funding Opportunity Announcement 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 forms package associated with this FOA includes all applicable components, mandatory and optional. Please note that some components marked optional in the application package are required for submission of applications for this FOA. Follow the instructions in the SF 424 (R&R) Application Guide to ensure you complete all appropriate "optional" components.
In conjunction with the SF424 (R&R) components, CDC grants 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. These forms can be downloaded from http://grants.nih.gov/grants/forms.htm

3. Letter of Intent

Due Date for Letter of Intent: **01/29/2020**
Although a letter of intent is not required, is not binding, and does not enter into 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 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 (identify the component you are applying to)
- 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 sent to:

National Center for Chronic Disease and Health Promotion (NCCDPHP) and NCBDDD

Extramural Research Program Operations and Services (ERPOS)

Marcella Law

Scientific Program Official

Extramural Research Program Operations and Services

Centers for Disease Control and Prevention

4770 Buford Highway, NE M/S F-80

Atlanta, GA 30341

Telephone: (770)-488-5416
Email: mah7@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.

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 16 components. Not all 16 components of the Research Plan apply to all Funding Opportunity Announcements (FOAs). Specifically, some of the following 16 components are for Resubmissions or Revisions only. See Part I, Section 5.5 of the SF 424 (R&R) Application
Guide (http://grants.nih.gov/grants/funding/424/SF424_RR_Guide_General_VerC.pdf) for additional information. Please attach applicable sections of the following Research Plan components as directed in Part 2, Section 1 (Funding Opportunity Announcement Description). Follow the page limits stated in the SF 424 unless otherwise specified in the FOA. As applicable to and specified in the FOA, 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 FOA.
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 timeline.
4. Inclusion Enrollment Report (Renewal and Revision applications ONLY)
5. Progress Report Publication List (for Continuation ONLY)

Human Subjects Section

6. Protection of Human Subjects
7. Inclusion of Women and Minorities
8. Targeted/Planned Enrollment Table (for New Application ONLY)

9. Inclusion of Children

Other Research Plan Sections

10. Vertebrate Animals
11. Select Agent Research
12. Multiple PD/PI Leadership Plan.
13. Consortium/Contractual Arrangements
14. Letters of Support
15. Resource Sharing Plan(s)
16. Appendix

Component 4 (Inclusion Enrollment Report) applies only to Renewal and Revision applications for clinical research. Clinical research is that which is conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies). Follow the page limits in the SF 424 **unless otherwise specified in the FOA.**
All instructions in the SF424 (R&R) Application Guide (http://grants.nih.gov/grants/funding/424/SF424_RR_Guide_General_VerC.pdf) must be followed along with any additional instructions provided in the FOA.

Research Plan

The applicant?s research plan should address activities that will be conducted over the entire five year project period and should include the following items:

Component A ? Coordination of the Longitudinal Database

- Describe a plan that includes a national coordinator that will provide technical assistance to the fragile X specialty clinics to:
    - support and encourage the collection of longitudinal data;
        - support collection of additional data points on participants enrolled in the longitudinal database;
        - support enrollment of new participants with fragile X syndrome.
    - manage communication between sites participating in the longitudinal database, the Data Coordinating Center (Component B), other partners (such as, but not limited to, the Fragile X Clinical and Research Consortium), and the clinics funded under Component C.
    - maintain a repository for all documents pertaining to the longitudinal database.
    - ensure satisfactory participation in the longitudinal database by conducting site visits and monitoring participation; assist sites with trouble shooting as needed.
- Describe a plan to ensure the collection of four additional data points on at least 150 individuals with fragile X syndrome already enrolled in the longitudinal database; three additional data points on at least 175 enrollees; two additional data points on at least 225 enrollees; and enroll at least 450 new participants (all ages) with fragile X syndrome into

the database.

- Describe a plan to collaborate with the Data Coordinating Center (Component B) to assist and monitor participating sites? IRB requests/approvals for participation in the longitudinal database.
- Describe a plan to document and provide a de-identified list of patients that attended the clinics participating 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.
- Describe a plan, including what entities you will collaborate with (e.g. Fragile X Clinical and Research Consortium, National Fragile X Foundation, FRAXA Research Foundation), to identify a common set of variables for the adult/aging FXS population ? particularly related to the needs of this population (i.e. clinical, occupational, familial, sociocultural, and caregiver needs issues such guidance regarding guardianship).
- Describe a plan to develop and pilot data collection on the adult population that can address questions such as: where do adults seek specialized care, what are the most common medical and psychosocial problems in the adult population, how does aging influence the health of individuals living with FXS, what services are used and needed in the adult population, and whether caregiver and guardianship challenges change? Data sources may include, but are not limited to: clinical, social, vocational, economic, housing and guardianship.
- Describe the methods that will be used to identify and recruit adult FXS patients.
- Describe strategies that will be implemented to engage new partners that care for the adult FXS population and describe how new clinics or other organizations involved with the adult FXS population will participate.
- If proposing clinic compensation for participation in the longitudinal database, describe the compensation plan ONLY for clinics not compensated through Component C.
- Applicants must have an established relationship with fragile X specialty clinics and describe how they will interact with the fragile X specialty clinics to support the collection of longitudinal data.
- Describe the applicant?s willingness to collaborate with the PIs of Component B and C and CDC representatives to establish and implement guidelines and processes for data analysis and publications. The goals of which should include, but are not limited to:
    - assuring and expediting orderly and timely presentation to the scientific community of all pertinent data resulting from the longitudinal database;
    - promoting accurate and scientifically sound presentations and papers from the longitudinal database;
    - promoting collaboration among clinicians and researchers participating in the longitudinal database and assuring that all participating sites have the opportunity to be involved in data analysis and the preparation of presentations and publications;
    - assuring press releases, presentations, and publications related to the longitudinal database are accurate and objective, and do not compromise the collaborative study and the acceptance of its results;
    - establishing guidelines for authorship, acknowledgments, and funding citations for any presentations and publications based on the longitudinal database.
- Describe the applicant?s willingness to collaborate with the Data Coordinating Center

(Component B) and participating clinicians and researchers in order to guide analyses that can address important clinical care and public health research questions and provide essential information to assist health care and allied professionals in providing better care, with the long-term goal of improving health outcomes and quality of life across the lifespan.

- Describe a plan for disseminating findings and sharing results with other fragile X specialty clinics; this may include collaborating with the Fragile X Clinical and Research Consortium.
- Describe willingness to collaborate with CDC to develop and implement an evaluation plan. The evaluation plan may include, but is not limited to, assessment of 1) logistics of data collection; 2) documentation of enrollment and non-enrollment; 3) data quality and data preparation for analyses; and 4) the utility of the information gathered to answer clinical care and public health research questions.
- Describe the approach to develop a sustainability plan for the maintenance and support of the longitudinal database beyond the completion of this FOA.

Component B ? Data Coordinating Center

- Describe the infrastructure and expertise available to develop and implement a data management and analysis center for receipt, processing, and analysis of patient, parent, clinician, and laboratory reported data from the participating clinics/sites or other data sources. The application must address:

1. Data security,
2. Data quality management,
3. Interface with existing data in the longitudinal database
4. System development and maintenance,
5. Staff capabilities,
6. Site and user support,
7. Data sharing and availability
    a. Describe the plan for establishing at least one, and no more than two, fixed datasets per year for the purpose of conducting analyses.

        i. Describe the plan to develop a ?data dictionary? or ?documentation of data? to accompany each dataset.

        ii. Describe a plan for providing the clinics contributing to the longitudinal database access to the annual or bi-annual fixed dataset(s).

        iii. Describe a plan for providing a copy of these de-identified fixed datasets(s) to CDC.

    b. Describe the plan for establishing a final public use dataset within two years of completing the five-year Cooperative Agreement.

8. Data analysis and visualization support.

- Describe the processes for protecting human subjects, including protecting personal

identifying information.

- Describe a plan to collaborate with the national coordinator (Component A) to assist and monitor participating sites? IRB requests/approvals for participation in the longitudinal database.
- Describe approach to conducting ongoing quality control/quality assurance to maintain high quality data.
- Describe the process for conducting at least one comprehensive review of the data every year to assess data quality.
- Describe the plan to collaborate with clinicians and researchers to conduct analyses using established clean, fixed annual or bi-annual datasets.
- Describe the applicant?s willingness to collaborate with the PIs of Component A and C and CDC representatives to establish and implement guidelines and processes for data analysis and publications. The goals of which should include, but are not limited to:

    a. assuring and expediting orderly and timely presentation to the scientific community of all pertinent data resulting from the longitudinal database;

    b. promoting accurate and scientifically sound presentations and papers from the longitudinal database;

    c. promoting collaboration among clinicians and researchers participating in the longitudinal database and assuring that all participating sites have the opportunity to be involved in data analysis and the preparation of presentations and publications;

    d. assuring press releases, presentations, and publications related to the longitudinal database are accurate and objective, and do not compromise the collaborative study and the acceptance of its results;

    e. establishing guidelines for authorship, acknowledgments, and funding citations for any presentations and publications based on the longitudinal database.

- Describe the applicant?s willingness to collaborate with the national coordinator (Component A) and participating clinicians and researchers in order to conduct analyses that can address important clinical care and public health research questions and provide essential information to assist health care and allied professionals in providing better care, with the long-term goal of improving health outcomes and quality of life across the lifespan.
- Describe the applicant?s willingness to collaborate with CDC to develop and implement an evaluation plan. The evaluation plan may include, but is not limited to, assessment of 1) logistics of data collection; 2) documentation of enrollment and non-enrollment; 3) data quality and data preparation for analyses; and 4) the utility of the information gathered to answer clinical care and public health research questions.
- Describe the applicant?s approach to develop a sustainability plan for the maintenance and support of the longitudinal database beyond the completion of this FOA.

<u>Component C ? Enhanced Participation of Fragile X Specialty Clinics</u>

- Describe a plan to ensure that at least 85% of returning patients already enrolled in the longitudinal database are approached for follow-up data and at least 85% of patients currently not enrolled in the longitudinal database are approached to obtain complete baseline data.
- Describe a plan to document and provide a de-identified list of patients who attended the clinic, indicating how many patients were approached for participation, how many patients were not approached, and of those approached how many patients declined participation.
- Applicants can choose to focus on enhanced participation OR enhanced measurement, OR both.
    - If choosing to focus on enhanced participation (minority, underserved, and adult populations)
        - Describe the applicant?s access to these populations.
        - Describe a plan to increase participation of minority and underserved FXS populations in the longitudinal database, the plan should focus on increasing participation in years 1-3 of the award and analyzing/assessing and disseminating findings in year 4. Efforts to increase participation should continue through years 4-5.
        - Describe a staffing plan to accomplish the objectives of this activity. The plan should include collaborating with CDC and experts in the field on engaging minority and underserved populations.
    - If choosing to focus on enhanced measurement (outcome measures)
        - Describe which measure(s) from the list below will be tested. If choosing a measure not listed below describe the measure, previous validation studies (if any), and provide justification for the selection. Note: list was adapted from the 2012 NIH Outcome Measures Working Group (Berry ?Kravis et al. Outcome Measures for Clinical Trials in Fragile X Syndrome. Journal of Developmental & Behavioral Pediatrics. Vol. 34, No. 7, September 2013)
            - Pediatric Anxiety Rating Scale (PARS)
            - Connors/SNAP-IV
            - Repetitive Behavior Scale ? Revised
            - Standardized language sample procedures
            - Eye tracking
            - KiTAP
        - Describe why it is an important measure in the FXS population.
        - Describe the metrics that will be used.
        - Describe if data from the longitudinal database will be utilized and how.
        - Describe a staffing plan to accomplish the objectives of this activity. The plan should include researchers with expertise in the area of outcome measures as they relate to FXS.
        - Describe a plan to obtain the measure at least annually for the first three years of the award.
        - If applicable, describe the plan to compare the performance of the selected measure(s) with one of the standardized parent-report instruments on behavior and communication currently being collected as

part of the FORWARD database: SRS, SCQ, ABC-C.

- Describe a plan for disseminating findings and sharing results with other fragile X specialty clinics in years 4 and 5 of the Cooperative Agreement; this may include collaborating with the Fragile X Clinical and Research Consortium.
- Describe willingness to collaborate with CDC to develop and implement an evaluation plan. The evaluation plan may include, but is not limited to, steps to evaluate utility of identified measures for use in individuals living with FXS and the ability to implement developed plan for the recruit underserved individuals with FXS.

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 FOA must be followed. For this specific FOA, 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 35 pages for all appendices.

8. Format for Attachments

Designed to maximize system-conducted validations, multiple separate attachments are required for a complete application. When the application is received by the agency, all submitted forms and all separate attachments are combined into a single document that is used by peer reviewers and agency staff. Applicants should ensure that all attachments are uploaded to the system.
CDC requires all text attachments to the Adobe application forms be submitted as PDFs and that all text attachments conform to the agency-specific formatting requirements noted in the SF424 (R&R) Application Guide (Part I, Section 2) (http://grants.nih.gov/grants/funding/424/ SF424_RR_Guide_General_VerC.pdf).

9. Submission Dates & Times

Part I. Overview Information contains information about Key Dates. Applicants are encouraged to submit in advance of the deadline to ensure they have time to make any application corrections that might be necessary for successful submission.
Organizations must submit applications via Grants.gov (https://www.grants.gov), the online portal to find and apply for grants across all Federal agencies. The eRA Commons systems retrieve the application from Grants.gov and check the application against CDC business rules. If no errors are found, the application will be assembled in the eRA Commons for viewing by the applicant before moving on for further CDC processing.
If errors are found, the applicant will be notified in the eRA Commons. They must make required changes to the local copy of their application and submit again through Grants.gov.

Applicants are responsible for viewing their application in the eRA Commons to ensure accurate and successful submission.
Once you can see your application in the Commons, be sure to review it carefully as this is what the reviewer will see. Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (http:// grants.nih. gov/grants /guide/url_redirect .htm? id=11123).
Information on the submission process is provided in the SF424 (R&R) Application Guide.
Note: HHS/CDC grant submission procedures do not provide a period of time beyond the grant application due date 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).
The application package is not complete until it has passed the Grants.gov/eRA Commons validation process. This process and email notifications of receipt, validation or rejection may take two (2) business days.
Applicants are strongly encouraged to allocate additional time prior to the submission deadline to submit their applications and to correct errors identified in the validation process. Applicants are encouraged also to check the status of their application submission to determine if the application packages are complete and error-free. Applicants who encounter system errors when submitting their applications must attempt to resolve them by contacting the Grants.gov Contact Center (1-800-518-4726; support@grants.gov). If the system errors cannot be resolved, applicants must contact TIMS at 770-488-2700; ogstims@cdc.gov for guidance at least 3 calendar days before the deadline date.
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. This validation process may take as long as two (2) business days. A third and final e-mail message is generated once the applicant's application package has passed validation and the grantor has confirmed receipt of the application.

Unsuccessful Submissions: If an application submission was unsuccessful, ***the applicant*** must:
1. Track his/her submission and verify the submission status (tracking should be done initially regardless of rejection or success).

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

2. Check his/her emails from both Grants.gov and eRA Commons for rejection notices.

    a. If the deadline has passed, he/she should email the Grant Management Specialist listed in the NOFO (ogstims@cdc.gov) explaining why the submission failed. b. If there is time before the deadline, he/she should correct the problem(s) and resubmit as soon as possible.

Due Date for Applications: **02/20/2020**

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 (http:// www. whitehouse.gov/ omb/ grants_spoc).

11. Funding Restrictions

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

12. Other Submission Requirements and Information

Application Submission

Applications must be submitted electronically following the instructions described in the SF 424 (R&R) Application Guide. **PAPER APPLICATIONS WILL NOT BE ACCEPTED.**
Applicants must complete all required registrations before the application due date.
Section III.6 "Required Registrations" contains information about registration.
For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically (http://grants.nih.gov/grants/guide /url_ redirect.htm? id=11144).

Important reminders: All PD/PIs must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF 424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to CDC.

The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management (SAM). Additional information may be found in the SF424 (R&R) Application Guide.

If the applicant has an FWA number, enter the 8-digit number. Do not enter the letters "FWA" before the number. If a Project/Performance Site is engaged in research involving human subjects, the applicant organization is responsible for ensuring that the Project/Performance Site operates under and appropriate Federal Wide Assurance for the protection of human subjects and complies with 45 CFR Part 46 and other CDC human subject related policies described in Part II of the SF 424 (R&R) Application Guide and in the HHS Grants Policy Statement.
See more resources to avoid common errors and submitting, tracking, and viewing applications: http:// grants.nih. gov/grants/ Electronic Receipt /avoiding _errors.htm or http:// grants. nih.gov/grants/ Electronic Receipt/submit _app.htm
Upon receipt, applications will be evaluated for completeness by the CDC Office of Grants

Services (OGS) and responsiveness by OGS and the Center, Institute or Office of the CDC. Applications that are incomplete and/or nonresponsive will not be reviewed.

Section V. Application Review Information

1. Criteria

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

Overall Impact

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

Scored Review Criteria

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

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?

Components A, B and C:

- Does the project address an important problem related to the health and wellbeing of people with FXS?
- What is the potential impact of this work on the health and wellbeing of the population living with FXS?
- How will this work be influential in the fragile X clinical and research communities?

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?

Component A:

- Does the PI have a record of research which has advanced the field of FXS clinical care or public health research?
- Has the applicant demonstrated a track record of working with multiple FXS specialty clinics?
- Is the applicant?s past performance well suited to the project?
- Has the applicant demonstrated the willingness and ability to actively participate in project activities, collaborate with recipients of Components B and C, and assume an active role in the Steering Committee that is intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C?

Component B:

- Does the PI have a record of participating in research which has advanced the field of FXS clinical care or public health research?
- Has the applicant demonstrated a track record of working with multiple FXS specialty clinics?
- Is the applicant?s past performance well suited to the project?
- Has the applicant demonstrated a track record of working with large databases and handling data from multi-site research projects?
- Has the applicant demonstrated the willingness and ability to actively participate in project activities, collaborate with recipients of Components B and C, and assume an active role in the Steering Committee that is intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C?

Component C:

- Does the PI have a record of research which has advanced the field of FXS clinical care or public health research?
- Has the applicant demonstrated the willingness and ability to assume active participation and take on leadership roles in ensuring participation in the projects?
- If the applicant chose to focus on minority and underserved populations, has the applicant demonstrated the ability to guide this work?
- If the applicant chose to focus on Outcome Measures, has the applicant demonstrated the ability to guide this work?
- Has the applicant demonstrated the willingness and ability to actively participate in project activities, collaborate with recipients of Components B and C, and assume an active role in the Steering Committee that is intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure

successful completion of Components A, B, and C?

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?

Component A, B and C:

- Does the project have the potential to improve the care of people affected by FXS?
- Does the application seek to inform current research or clinical practice by contributing to the collection and analysis of longitudinal data?

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?

Component A:

- Has the applicant demonstrated an effective plan to ensure participation in the longitudinal database? Is the plan sufficient to ensure the collection of four additional data points on at least 150 individuals with fragile X syndrome already enrolled in the longitudinal database; three additional data points on at least 175 enrollees; two additional data points on at least 225 enrollees; and enroll at least 450 new participants (all ages) with fragile X syndrome into the longitudinal database?
- Has the applicant demonstrated a sufficient plan to develop and pilot data collection in the adult population?
- Has the applicant provided a detailed plan for overseeing a national coordinator that can provide technical assistance to the clinics?
- Does the national coordinator have experience coordinating multi-site data collection?
- Are the partner(s) identified by the applicant adequate to accomplish the goals and objectives? Does the applicant have a sufficient plan to engage partner(s)? Does the

applicant have documented support from the partner(s)?

Component B:

- Has the applicant demonstrated a sufficient plan to properly receive, process, secure, manage and analyze data?
- Has the applicant demonstrated a plan to provide data sets to be used for analyses (there must be at least one and no more than two data sets per year)?
- Has the applicant demonstrated a detailed and feasible plan to evaluate data quality?
- Has the applicant provided a detailed staffing and resources plan, including a description of the staff commitments and necessary expertise of staff to operate as the Data Coordinating Center?

Component C:

- Has the applicant demonstrated a feasible plan to ensure participation in the longitudinal database?
- Has the applicant demonstrated a sufficient plan to either 1) increase participation of minority and underserved populations in the longitudinal database OR, 2) pilot a tool to measure cognitive or behavioral function in FXS patients? Please note: applicants can choose to address 1 or 2 or both 1 and 2.
- Has the applicant provided a detailed staffing and resources plan, including a description of the staff commitments and necessary expertise of staff to carry out the research plan?

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?

Component A and B:

- Has the applicant demonstrated the ability to work with multiple FXS specialty clinics to support data collection for the longitudinal database? Are there letters of support from the FXS specialty clinics?
- 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?
- Has the applicant demonstrated a plan to share results with the fragile X clinical and research communities?

Component C:

- 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?
- Has the applicant demonstrated a plan to share results with the fragile X clinical and research communities?

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 and the policy on the Inclusion of Persons Under 21 in Research (https://www.cdc.gov/maso/Policy/policy496.pdf).

Vertebrate Animals The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information on review of the Vertebrate Animals section, please refer to the

Worksheet for Review of the Verterbrae Animal Section
(https://grants.nih.gov/grants/olaw/VAChecklist.pdf).

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

Dual Use Research of Concern Reviewers will identify whether the project involves one of the agents or toxins described in the US Government Policy for the Institutional Oversight of Life Sciences Dual Use Research of Concern, and, if so, whether the applicant has identified an IRE to assess the project for DURC potential and develop mitigation strategies if needed.
For more information about this Policy and other policies regarding dual use research of concern, visit the U.S. Government Science, Safety, Security (S3) website at: http://www.phe.gov/s3/dualuse. Tools and guidance for assessing DURC potential may be found at: http://www.phe.gov/s3/dualuse/Pages/companion-guide.aspx.

3. Additional Review Considerations

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

HHS/CDC will assess the reasonableness of the data sharing plan. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The presence of a data sharing plan will be part of the terms and conditions of the award. The funding organization will be responsible for monitoring the data sharing policy.

Data sharing agreement

Awardees will retain custody of and have primary rights to their data developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies. The collaborative protocol and governance policies will call for the participating sites to submit de-identified data for the longitudinal database to the Data Coordinating Center; the submission of copies of the de-identified datasets to CDC; procedures for data analysis, reporting and publication; and procedures to protect and ensure the privacy of medical and genetic data (if any) and records of individuals. The study will be expected to put all study materials and procedures manuals in the public domain and/or make them available to qualified investigators. Awardees are encouraged to publish and to publicly release and disseminate results, data and other products of the study, concordant with the study protocol and governance and the approved plan for making data and materials available to the scientific community.

Resource Sharing Plans 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: http://www.cdc.gov/grants/additionalrequirements/index.html. Investigators responding to this funding opportunity should include a plan on sharing research resources and data.

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

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 decisions:

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

.Component C: Diversity of project focus (outcome measures and targeting minority or underserved)

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 recipient's business official.

Recipients 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.

NOFO Recipients must comply with administrative and national policy requirements as appropriate. For more information on the Code of Federal Regulations, visit the National Archives and Records Administration: http://www. access.gpo.gov/ nara/cfr/cfr-table-search.html.

Specific requirements that apply to this NOFO are the following:

AR-1: Human Subjects Requirements

AR-2: 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: Release and Sharing of Data

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 - Distinguishing Public Health Research and Public Health Non-research

AR 32 – FY 2012 Enacted General Provisions

ARs applicable to HIV/AIDS Awards:

AR-4: HIV/AIDS Confidentiality Provisions

AR-5: HIV Program Review Panel Requirements

AR-6: Patient Care

ARs applicable to ATSDR Awards:

AR-18: Cost Recovery – ATSDR

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

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

For more information on the Code of Federal Regulations, visit the National Archives and Records Administration at: http://www.access.gpo.gov/nara/cfr/cfr-table-search.html

To view brief descriptions of relevant CDC requirements visit: http://www.cdc.gov/od/pgo/funding/grants/additional_req.shtm

3. Additional Policy Requirements

The following are additional policy requirements relevant to this FOA:

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: http://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.

4. Cooperative Agreement Terms and Conditions of Award

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 Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), 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 Recipents 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 Officer 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 Recipents for the project as a whole, although specific tasks and activities may be shared among the Recipents and HHS/CDC as defined below.

Recipents 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.

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

Component A:

- Providing oversight of all management, administrative, and scientific aspects of the project in collaboration with the fragile X specialty clinics.
- Providing oversight of the national coordinator.
- Serving on an overarching Steering Committee intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site from Components A, B, and C and CDC staff.
- Participating in other committees and workgroups that work across components A, B, and C.
- Collaborating with the Data Coordinating Center (Component B) to obtain and maintain the appropriate Institutional Review Board approvals for all institutions or individuals participating in the research project; and provide this documentation to CDC as required.
- Ensuring timely responses to all Quality Assurance/Quality Control (QA/QC).
- Working collaboratively with CDC to develop and finalize the research protocol, research agenda, and data sharing agreement that details data use, access, sharing of de-identified data with CDC collaborators, publication plan, and review of analyses.
- Adhering to established Publication and Data Sharing Guidelines.
- Providing accurate and timely reports, per guidance in the “Reporting” section below.

Component B:

- Providing oversight of all management, administrative, and scientific aspects of the

project in collaboration with the fragile X specialty clinics.

- Providing training to fragile X specialty clinics to promote efficient data collection and support clinics to send de-identified data to the data management and analysis center.
- Collaborating with the national coordinator (Component A) to obtain and maintain the appropriate Institutional Review Board approvals for all institutions or individuals participating in the research project; and provide this documentation to CDC as required.
- Ensuring a de-identified dataset is shared with CDC at least annually.
- Serving on an overarching Steering Committee intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site from Components A, B, and C and CDC staff.
- Participating in other committees and workgroups that work across components A, B, and C.
- Working collaboratively with CDC to develop and finalize the research protocol, research agenda, and data sharing agreement that details data use, access, sharing of de-identified data with CDC collaborators, publication plan, and review of analyses.
- Adhering to established Publication and Data Sharing Guidelines.
- Providing accurate and timely reports, per guidance in the "Reporting" section below.

Component C:

- Providing oversight of all management, administrative, and scientific aspects of the project.
- Collaborating with the recipients of Components A and B to submit de-identified data for the longitudinal database.
- Obtaining and maintaining the appropriate Institutional Review Board approvals for all institutions or individuals participating in the research project; and provide this documentation to CDC as required.
- Serving on an overarching Steering Committee intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site from Components A, B, and C and CDC staff.
- Participating in other committees and workgroups that work across components A, B, and C.
- Working collaboratively with CDC to develop and finalize the research protocol, research agenda, and data sharing agreement that details data use, access, sharing of de-identified data with CDC collaborators, publication plan, and review of analyses.
- Providing accurate and timely reports, per guidance in the "Reporting" section below.

HHS/CDC Responsibilities:

An HHS/CDC Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

There are two separate CDC scientific roles – Scientific Collaborator (SC) and Scientific Program

Official SPO). In this cooperative agreement, a NCBDDD SC is an equal partner with scientific and programmatic involvement during the conduct of the project through technical assistance, advice, and coordination.

The SC will:

- Provide expertise and guidance on the project.
- Support the recipients' activities in data collection, management, and analysis.
- Assist in the analyses, interpretation, and reporting of findings in the literature.
- Serve as a one of the CDC representatives on the overarching Steering Committee intended to provide guidance and expertise with regard to successful completion of Components A, B, and C. Members of the Steering Committee must include the PIs from Components A, B, and C and CDC representatives. Participate in the QA/QC activities;
- Collaborate with the recipient to implement the evaluation plan.

Additionally, an HHS/CDC NCBDDD Project Officer or other HHS/CDC staff will provide day-to-day programmatic, administrative, and fiscal management in support of the project as defined above.

CDC Extramural Research Program Operations and Services (ERPOS) will appoint a Scientific Program Official (SPO), apart from the NCBDDD Scientific Collaborator. The CDC SPO will be responsible for the normal scientific and programmatic stewardship of the award.

The SPO 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.
- Assure 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:

- Collaborate with leadership from each of the Components, CDC representatives, and other individuals and organizations as applicable.
- Participating on a Steering Committee intended to encourage collaboration across components of this FOA and provide the necessary expertise and oversight to ensure successful completion of Components A, B, and C. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site from Components A, B, and C and CDC staff. The Steering Committee may consider adding non-voting liaisons from patient oriented organizations from patient oriented organizations, including but not limited to, the National Fragile X Foundation and FRAXA Research Foundation. Additional non-voting members must be unanimously approved by the designated Steering Committee members described above.

    a. Each year the Chair of the Steering Committee shall be elected by the members of the Steering Committee and serve on a rotating basis; the Chair must

be one of the PIs for Components A, B, and C. Each PI shall serve as Chair for at least one, and no more than two, years.

b. The Steering Committee should meet at least monthly by phone for the duration of the Cooperative Agreement, and may be required to meet more frequently as needed.

c. The Steering Committee shall meet in-person at least once per year for the duration of the Cooperative Agreement.

- Recipents of Components A, B, and C will be expected to communicate regularly with one another and the CDC. This could include, but is not limited to, monthly calls, in-person meetings, webinars, and email communication.
- Recipents of Components A, B, and C shall coordinate at least one in-person grantee meeting each year.
- Recipents of Components A, B, and C shall work together to conduct analyses and develop presentations and publications for the scientific and lay audiences.
- Collaborate with clinicians and researchers from the sites participating in the longitudinal database, the PIs of Components A, B and C, and CDC representatives to identify important clinical care and public health research questions and utilize data from the longitudinal database to address them.
- Collaborate with the PIs of Component A, B, and C and CDC representatives to establish and implement guidelines and processes for data analysis and publications.
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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 required and must be submitted through eRA Commons **within 90 days after the end of the calendar quarter in which the budget period ends.**

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

B. Content of Reports

1. Yearly Non-Competing Grant Progress Report: The grantee's continuation application/progress report should include:

- Description of Progress during Annual Budget Period: Current Budget Period Progress reported on the PHS 2590 (http:// grants1.nih.gov/ grants/funding/ 2590/2590.htm) http:// grants.nih.gov/grants/ funding/2590/2590.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.

Section VII. Agency Contacts

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

Application Submission Contacts

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

eRA Commons Help Desk (Questions regarding eRA Commons registration, tracking application status, post submission issues, FFR submission)
Phone: 301-402-7469 or 866-504-9552 (Toll Free)
TTY: 301-451-5939
Email: commons@od.nih.gov
Hours: Monday - Friday, 7am - 8pm U.S. Eastern Time

CDC Technical Information Management Section (TIMS)
Telephone 770-488-2700

Email: ogstims@cdc.gov
Hours: Monday - Friday, 7am – 4:30pm U.S. Eastern Time

Scientific/Research Contact(s)

Marcella Law
Scientific Program Official
Extramural Research Program Operations and Services

Centers for Disease Control and Prevention
4770 Buford Highway, NE Mailstop F-80
Atlanta, GA 30342
Telephone: (770)-488-5416
Email: mah7@cdc.gov

Peer Review Contact(s)

Jaya Raman, Ph.D.

Scientific Review Official

Extramural Research Program Operations and Services

Centers for Disease Control and Prevention
4770 Buford Highway, NE Mailstop F-80
Atlanta, GA 30342
Telephone: (770)-488-6511
Email: kva@cdc.gov

Financial/Grants Management Contact(s)

Sharon Cassell

Grants Management Officer

Office of Financial Resources (OFR)

Office of Grant Services (OGS)

Telephone: 770-488-2703

Email: zpr0@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.

Appendix A: Supplemental funding opportunity: Using Longitudinal Data to Characterize the Natural History of Fragile X Syndrome to Improve Services and Outcomes

RFA-DD-15-003

Application Due Date: 02/20/2020

Activity Code

U01 Amendment 1 made on February 10, 2015

Funding Opportunity Announcement Type

Reissue of CDC-RFA-DD-15-003
Health

Purpose

This supplement funding opportunity provides supplemental funding to existing recipients under CDC-RFA-15-003 to maximize the value of research activities currently underway. The activities supported with this supplemental funding are expected to enhance completed research under Component A and B of CDC-RFA-15-003, "Using Longitudinal Data to Characterize the Natural History of Fragile X Syndrome to Improve Services and Outcomes." It supports the maintenance and expansion of the Forward Online Registry with Accessible Research Database (FORWARD) and allows for increased participation among adults with fragile X syndrome (FXS). Supplemental funding applications are requested to continue and complete longitudinal data collection for FORWARD, from individuals currently enrolled in the database and from new enrollees. The proposed research activities for supplemental funding must complement and build on research activities previously completed under CDC-RFA-15-003, to contribute to the characterization of the population with (FXS) and to assess the impact of the condition on the health and quality of life of those affected across their lifespan. This supplemental funding will support the following:

Component A: The purpose of Component A is to maintain and expand the current FORWARD dataset, to coordinate efforts to expand the age range covered by this dataset to enable researchers to describe the natural history of FXS across the life span and to characterize the long-term impact of interventions and treatments on both health outcomes and quality of life.

Component B: The purpose of Component B is to support a Data Coordinating Center that will receive, process, and analyze the data from patients, parents, clinicians, and laboratories as reported from clinics participating in the FORWARD longitudinal database and from other sources.

Key Dates

Publication Date:

To receive notification of any changes to RFA-DD-15-003, 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: **01/29/2020**

Application Due Date: 02/20/2020

On-time submission requires that electronic applications be error-free and made available to CDC for processing from eRA Commons on or before the deadline date. Applications must be submitted to and validated successfully by Grants.gov/eRA Commons no later than 5:00 PM U.S. Eastern Time. Note: HHS/CDC grant submission procedures do not provide a period of time beyond the application due date 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: 04/06/2020
The 04/06/2020 date listed above is an approximate date for this supplemental funding opportunity.

Secondary Review: 04/06/2020

Estimated Start Date: **09/01/2020**

Estimated Start Date for this supplemental funding opportunity: September 1, 2020.

Expiration Date: 02/21/2020
Due Dates for E.O. 12372: Executive Order 12372 does not apply to this program.

Required Application Instructions

It is critical that applicants follow the instructions in the SF 424 (R&;R) Application Guide except where instructed to do otherwise in this FOA. Conformance to all requirements (both in the Application Guide and the FOA) 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.

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

Executive Summary

Purpose. This supplemental funding opportunity will provide FY 20 funds to extend the project period for Component A and B to support the maintenance and expansion of the Forward Online Registry with Accessible Research Database (FORWARD) to increase participation in the longitudinal database, particularly among adults with FXS. The purpose of the supplement is to contribute to the characterization of the population with fragile X syndrome (FXS) and to assess the impact of interventions and treatments on the health and quality of life of those

affected across their lifespan.

Funds Available and Anticipated Number of Awards. The estimated total level of funding (direct and indirect for entire project period in dollars) that is available for the supplement is $550,000. Component A: The estimated total funding (direct and indirect) for the one-year project is $350,000. It is anticipated that one award will be made to a single recipient in FY 2020. Component B: The estimated total funding (direct and indirect) for the one year is $200,000. It is anticipated that one award will be made to a single recipient in FY 2020.

Awards issued under this are contingent upon availability of funds.

Budget and Project Period. The estimated total funding (direct and indirect) for the entire project period, September 1, 2020-August 31, 2021, is $550,000. For Component A, the anticipated award amount for the budget period is $350,000 (direct and indirect). For Component B, the anticipated award amount for the budget period is $200,000 (direct and indirect).

Application Type: Supplemental Funding Opportunity

Part 2. Full Text

Section I. Funding Opportunity Description

Statutory Authority

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

1. Background and Purpose

The purpose of this NOFO is to provide supplemental funding to extend existing Components A and B projects:

Component A - Coordination of the Longitudinal Database

The purpose of Component A is to maintain and expand the current FORWARD dataset, to coordinate efforts to expand the age range covered by this dataset to enable researchers to describe the natural history of FXS across the life span and to characterize the long-term impact of interventions and treatments on both health outcomes and quality of life. Component A will continue the collection of data for the FORWARD longitudinal database with special emphasis in two areas: 1) collect follow-up data on individuals already enrolled and 2) collect data on newly enrolled participants, particularly on minority and underserved populations and adults with FXS over 24 years of age.

The purpose of Component B is to support a Data Coordinating Center that will receive, process, and analyze the data from patients, parents, clinicians, and laboratories as reported from clinics participating in the FORWARD longitudinal database and from other sources. The scope of this supplement is reduced compared with that of CDC-RFA-DD-15-003 in that it does not support funding for Component C. Component C projects were intended to be of limited timeframe. The purpose of Component C was two pronged: (1) to improve participation of minority and underserved populations in the longitudinal registry and (2) to test approaches for measuring cognitive and behavioral measures. The purpose and intent of the component will have been accomplished by the conclusion of the project period for CDC-RFA-DD-15-003.

Public Health Impact

FXS is a lifelong condition; therefore, there is a need to address long-term goals such as improving health outcomes and quality of life and filling knowledge gaps regarding the changing health status of people living with FXS and the effectiveness of the interventions that may improve this status. We currently know little about interventions and treatments that yield the best outcomes. To date, research efforts have primarily focused on children, therefore not much is known about the health status and social wellbeing of adults living with FXS - where they seek specialized care, how aging influences the services they use and need, and whether they face challenges with changes of caregivers and guardianships. Because this project includes affected individuals at various developmental stages, it can provide a much-needed epidemiologic profile of the FXS population across the lifespan for the first time, which may lead to the development of effective interventions and services. The inclusion of minority and underserved populations will create a better description of the FXS clinic-based population and will provide preliminary data to investigate health disparities among population subgroups.

Relevant Work

This work will build on three studies, the first two were pilot studies. The first pilot study (2008-2011) tested the infrastructure required to implement multi-site research in FXS; it proved that the Fragile X Clinical and Research Consortium (FXCRC) successfully facilitated research across multiple FXS specialty clinics. The second pilot study (2011-2015) tested the feasibility of longitudinal data collection. During this 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 the Fragile X Online Registry With Accessible Research Database (FORWARD). Data for the Registry and Database were provided 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). More information about the clinics can be found at www.fxcrc.org. The third study (2015-2020) continued the work established in the pilot studies, expanding data collection for FORWARD and enabling (multi-year) longitudinal data collection for existing and new participants. This study emphasized the enrollment of minority and underserved populations and of 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. he expansion of the collection of epidemiologic data allows a more robust and inclusive description of the FXS population.

2. Approach

The work specified in this supplement should build on previous efforts to implement the FORWARD Registry and Database as well as address gaps in knowledge identified by a previous structured literature review and input from stakeholders and FXS experts. This supplement will continue the expansion of the FORWARD database to include adults living with FXS and will encourage participation of underserved and minority populations. To refine the characterization of the FXS population, the work shall include, without limiting it to, data collection on variables relevant to individuals living with FXS at various developmental stages. This supplement has two separate components aimed at collecting and analyzing data that can provide a robust description of the FXS population, an informed understanding of the natural history of FXS across the lifespan, and an analysis of the impact of treatments and interventions

on health outcomes and quality of life.

Objectives/Outcomes

One-Year Objectives/Outcomes

Component A - Coordination of the Longitudinal Database: Outcomes

Component A will utilize a national coordinator to support and coordinate data collection activities across fragile X specialty clinics and facilitate the expansion of the longitudinal database to include adults living with FXS. The national coordinator may collaborate with the Fragile X Clinical Research Consortium (FXCRC) to facilitate access to study participants from the specialty clinics. The national coordinator will collaborate with the Data Coordinating Center to ensure timely and accurate data collection.

Component A - Coordination of the Longitudinal Database: One-Year Objectives

- Using the data collection tools of the FORWARD Registry and Database, expand on longitudinal data by collecting one additional follow-up data point on at least 100 individuals with fragile X syndrome enrolled in FORWARD and baseline data on at least 90 new individuals.
- Obtain new data specific to the adult FXS population - clinical and social services used and needed across the lifespan as well as possible occupational, familial, sociocultural, and guardianship factors that need to be addressed along with other caregiver needs.
- Collaborate with clinicians and researchers from the sites participating in the longitudinal database, the PI of Component B, and CDC representatives to identify important clinical care and public health research questions and utilize data from the longitudinal database to address them.
- Collaborate with the PI of Component B and CDC representatives to establish and implement guidelines and processes for data analysis and publications.
- Participate in a Steering Committee that is intended to encourage collaboration across components of this supplement and provide the necessary expertise and oversight to ensure successful completion of the objectives in Components A and B. Members of the Steering Committee will be comprised of PIs, or co-PIs, from each awarded site and CDC staff. The Steering Committee may consider adding non-voting liaisons from patient-oriented organizations, including but not limited to, the National Fragile X Foundation and FRAXA Research Foundation. The Steering Committee may include non-voting members and PIs for current recipients of DD-15-003. Addition of non- voting members must be unanimously approved by the designated Steering Committee members described above.
- Develop a sustainability plan for activities specified under Component A after this one-year project period ends.

Component B - Data Coordinating Center: Outcomes

Component B will support a Data Coordinating Center to build on the existing longitudinal database to maintain and manage data collected by participating clinics.

Component B - Data Coordinating Center: One-Year Objectives

- Build on the existing longitudinal database by receiving, processing, and analyzing patient,
parent, clinician, and laboratory reported data from the participating clinics or other data

sources.
• Conduct ongoing quality control/quality assurance to maintain high quality data.
• Combine data from participating sites and create at least one de-identified dataset used for analysis.
• Issue a data dictionary or documentation of data to accompany each dataset.
• Collaborate with the PI of Component A and CDC representatives to establish and implement guidelines and processes for data analysis and publications.
• Work with clinicians and researchers participating in the longitudinal database to conduct analyses and publish findings.
• Participate in a Steering Committee that is intended to encourage collaboration and provide the necessary expertise and oversight to ensure successful completion of Components A and B.
• Collaborate with clinicians and researchers to conduct analyses using an established dataset (i.e., created prior to the funding cycle) or a newly-created cleaned dataset.
• Develop a sustainability plan for activities specified under Component B after this one-year project period ends.

Target Population

The target population for this supplement funding opportunity includes individuals diagnosed with FXS, all ages, currently attending an FXS specialty clinic or not attending an FXS specialty clinic but meeting the criteria to be attending. Data contributions will come from FXS specialty clinics; other clinics that provide care to FXS patients; and individual fragile X clinicians and researchers.

Collaboration/Partnerships

Recipients of Components A and B are expected to collaborate with one another, with the FXS specialty clinics (which may include collaboration with the Fragile X Clinical and Research Consortium), and with the CDC to accomplish the goals and objectives stated in this supplement. The recipients of Component A will be expected to collaborate with fragile X organizations such as, but not limited to, The National Fragile X Foundation and FRAXA Research Foundation.

Evaluation/Performance Measurement

Recipients of Components A and B are expected to participate in the planning and implementation of a program evaluation of the longitudinal database in collaboration with CDC.

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 mechanisms available (e.g. social media).

OMB/PRA may not apply.

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:

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

Estimated Total Funding: $550,000
Funding will be awarded as a supplement to existing award. The supplemental funding level (direct and indirect costs) for the one-year budget period, September 1, 2020-August 31, 2021 is $550,000, and the estimated total supplemental funding level (direct and indirect) for the entire one-year period of performance is $550,000. Component A, the estimated total supplemental funding amount for the one-year budget period, September 1, 2020 - August 31, 2021, is $350,000 (direct and indirect). For Component B, the estimated total supplemental funding amount for the one-year budget period, September 1, 2020 - August 31, 2021, is $200,000 (direct and indirect).

Anticipated Number of Awards: 2
Component A, the estimated total supplemental funding amount for the one-year budget period, September 1, 2020 - August 31, 2021, is $350,000 (direct and indirect). Award Ceiling for Component A is $350,000 for the one-year Budget Period and the Award Floor is $0. For Component B, the estimated total supplemental funding amount for the one-year budget period, September 1, 2020 - August 31, 2021, is $200,000 (direct and indirect). Award Ceiling for Component B is $200,000 for the one-year Budget Period and the Award Floor is $0.It is anticipated that 1 award will be made to a single recipient for Component A and 1 award will be made to a single recipient for Component B.

Award Ceiling: $350,000 for Component A and $200,000 for Component B

Award Floor: $0 Per Project Period

Total Project Period Length: 1 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 (https://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.

5. Responsiveness
Each application, SF 424 (R&R), must include the correct Component number in Field 4.a. Federal Identifier and CDC grant number in Field 4.b. Agency Routing Identifier.
If an applicant needs to submit a revision to their supplemental application, they must enter their Grants.gov tracking number in Field 4.c. in addition to the information required above.

4.a. Federal Identifer: Component A

4.b. Agency Routing Identifer: DD00234

To be considered responsive to this announcement, applicants may not request funding above the ceiling amount of $350,000 for Component A and $200,000 for Component B (includes both direct and indirect costs).

If your application is incomplete or non-responsive to these requirements, it will not enter into the review process.

The applicant requesting supplemental funding under this announcement must be currently funded under CDC-RFA-15-003. Applications received from any other entity will not be forwarded for review.

6. Required Registrations

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

- (Foreign entities only): Special Instructions for acquiring a Commercial and Governmental Entity (NCAGE) Code: https://eportal.nspa.nato. int/AC135Public/Docs/US%20Instructions%2 0for%20NSPA%20NCAGE.pdf
- System for Award Management (SAM) – must maintain current registration in SAM (the replacement system for the Central Contractor Registration) to be renewed annually, https ://www.sam.gov/portal/SAM/#1.
- 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 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 registration process at least four (4) weeks prior to the application due date.

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/ asfr/ ogapa/ aboutog/ 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.

Section IV. Application and Submission Information

1. Address to Request Application Package

Applicants must download the SF424 (R&R) application package associated with this funding opportunity from www.Grants.gov.

If access to the Internet is not available or if the applicant encounters difficulty accessing the forms on-line, contact the HHS/CDC Office of Grants Services (OGS) Technical Information Management Section (TIMS) staff at (770) 488-2700 or ogstims@cdc.gov for further instructions. Hours: Monday - Friday, 7am – 4:30pm U.S. Eastern Time. CDC Telecommunications for the hearing impaired or disabled is available at: TTY 1-888-232-6348.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the SF424 (R&R) Application Guide (http://grants.nih.gov/grants/guide/url_redirect.htm?id=12000), except where instructed in this Funding Opportunity Announcement 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 forms package associated with this FOA includes all applicable components, mandatory and optional. Please note that some components marked optional in the application package are required for submission of applications for this FOA. Follow the instructions in the SF 424 (R&R) Application Guide to ensure you complete all appropriate "optional" components.
In conjunction with the SF424 (R&R) components, CDC grants 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. These forms can be downloaded from http://grants.nih.gov/grants/forms.htm

Application and Submission: Each application, SF 424 (R&R), must include the correct Component in Field 4.a. Federal Identifier and CDC award number in Field 4.b. Agency Routing Identifier. Field 4.c. should include Grants.gov tracking number if applicant is submitting a revised application.

Content and Form of Application Submission: Each application, SF 424 (R&R), must be submitted as a "Revision" Application (Field 8.) and must include the correct component number in Field 4.a. Federal Identifier and CDC grant number in Field 4.b. Agency Routing Identifier.

If applicant does not select "Revision," the application will not be submitted as a Type 2, as required.

A revision to an already submitted application is allowable, but it will replace the previously submitted application. Applicant must enter Grants.gov Tracking number in Field 4.c.

Only one application per institution (normally identified by having a unique DUNS number) per component is allowed. Applicants can apply for more than one component. If applying for more than one component, a separate application for each component is required.

Submission Dates & Times: Applicants are encouraged to submit early to ensure application passes submission validations.

3. Letter of Intent

Due Date for Letter of Intent: **01/29/2020**

Although a letter of intent is not required, is not binding, and does not enter into 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 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 (identify the component you are applying to)

- 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 sent to:
National Center for Chronic Disease and Health Promotion (NCCDPHP) and NCBDDD

Extramural Research Program Operations and Services (ERPOS)

Marcella Law

Scientific Program Official

Extramural Research Program Operations and Services

Centers for Disease Control and Prevention

4770 Buford Highway, NE M/S F-80

Atlanta, GA 30341

Telephone: (770)-488-5416

Email: mah7@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.

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 16 components. Not all 16 components of the Research Plan apply to all Funding Opportunity Announcements (FOAs). Specifically, some of the following 16 components are for Resubmissions or Revisions only. See Part I, Section 5.5 of the SF 424 (R&R) Application Guide (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 (Funding Opportunity Announcement Description). Follow the page limits stated in the SF 424 unless otherwise specified in the FOA. As applicable to and specified in the FOA, 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 FOA.
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 timeline.

4. Inclusion Enrollment Report (Renewal and Revision applications ONLY)
5. Progress Report Publication List (for Continuation ONLY)

Human Subjects Section

6. Protection of Human Subjects
7. Inclusion of Women and Minorities
8. Targeted/Planned Enrollment Table (for New Application ONLY)
9. Inclusion of Children

Other Research Plan Sections

10. Vertebrate Animals
11. Select Agent Research
12. Multiple PD/PI Leadership Plan.
13. Consortium/Contractual Arrangements
14. Letters of Support
15. Resource Sharing Plan(s)
16. Appendix

Component 4 (Inclusion Enrollment Report) applies only to Renewal and Revision applications for clinical research. Clinical research is that which is conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies). Follow the page limits in the SF 424 **unless otherwise specified in the FOA**.
All instructions in the SF424 (R&R) Application Guide (http://grants.nih.gov/grants/how-to-apply-application-guide/forms-d/general-forms-d.pdf) must be followed along with any additional instructions provided in the FOA.

The applicant's research plan should address activities that will be conducted over the entire one-year project and should include the following items:

Component A – Coordination of the Longitudinal Database

- Describe a plan that includes a national coordinator that will provide technical assistance to the FXS specialty clinics to:

  o support and encourage the collection of longitudinal data by

    - adding data points on participants already enrolled in the longitudinal database;
    - enrolling new participants with FXS, particularly adults with FXS.

  o manage communication between sites participating in the longitudinal database, the Data Coordinating Center (Component B) and other partners (such as, but not limited to, the Fragile X Clinical and Research Consortium).

  o maintain a repository for all documents pertaining to the work in building the longitudinal database.

- ensure satisfactory participation in the longitudinal database by conducting site visits and monitoring data contributions; assist sites with trouble shooting as needed.

- Describe a plan to ensure the collection of one additional follow-up data point on at least 100 individuals with FXS enrolled in FORWARD and baseline on 90 newly enrolled individuals.
- Describe a plan to collaborate with the Data Coordinating Center (Component B) to assist and monitor participating sites' IRB requests/approvals for participation in the longitudinal database.
- Describe a plan to document and provide a de-identified list of patients who attended the clinics and were approached for participation, provide the numbers of those who accepted and those who declined to participate in the study; and, if some patients were not approached, provide their number and reasons for not approaching them.
- Describe the methods that will be used to identify and recruit adult FXS patients.
- Describe strategies that will be implemented to engage new partners that care for the adult FXS population and describe how they will participate.
- If requiring clinic compensation in exchange for participating in the longitudinal database, describe the compensation plan.
- Applicants must have an established relationship with FXS specialty clinics and should describe how they will interact with these clinics to support the collection of longitudinal data.
- Describe the applicant's willingness to collaborate with the PI(s) of Component B and CDC representatives to implement guidelines and processes for data analysis and publications. The goals of which should include, but are not limited to:

  - assuring and expediting orderly and timely presentation to the scientific community of all pertinent results emerging from the analyses of the longitudinal database;

  - promoting accurate and scientifically sound presentations and papers involving the longitudinal database;

  - promoting collaboration among clinicians and researchers participating in the longitudinal database and assuring that all participating sites have the opportunity to be involved in data analysis and the preparation of presentations and publications;

  - assuring that press releases, presentations, and publications related to the longitudinal database are accurate and objective, and do not compromise the collaborative study and the acceptance of its results.

- Describe the applicant's willingness to collaborate with the Data Coordinating Center (Component B) and other participating clinicians and researchers in order to guide analyses that can address important clinical care and public health research questions. The goal is to deliver essential information that health care and allied professionals could use in providing better care and improving health outcomes and quality of life across the lifespan.
- Describe a plan for disseminating findings and sharing results with other fragile X specialty clinics; this may include collaborating with the Fragile X Clinical and Research Consortium.

- Describe willingness to collaborate with CDC to implement an evaluation plan. The evaluation plan may include, but is not limited to, assessment of 1) logistics of data collection; 2) documentation of enrollment and non-enrollment; 3) data quality and data preparation for analyses; 4) the utility of the information gathered to answer clinical care and public health research questions 5) project outcomes.
- Describe a sustainability plan for activities specified under Component A after this one-year project period ends.

Component B – Data Coordinating Center

• Describe the infrastructure and expertise available to develop and implement a data management and analysis center to receive, process, and analyze data submitted by patients, parents, clinicians, and other data sources.

The application must address:
1. Data security
2. Data quality management
3. Interface with existing data in the longitudinal database
4. System development and maintenance
5. Staff capabilities
6. Site and user support
7. Data sharing and availability

a. Describe the plan for making available at least one, no more than two, documented, de-identified datasets for analyses.

i. Describe the plan to develop an annotated data dictionary or data document to accompany dataset(s).
ii. Describe a plan for providing access to the dataset(s) to the clinics contributing to the longitudinal database.
iii. Describe a plan for providing a copy of these de-identified datasets(s) to CDC.

b. Describe the plan for preparing a final dataset within two years of completing the Cooperative Agreement.

8. Data analysis and visualization support.

• Describe the processes for protecting human subjects, including protecting personal identifying information.
• Describe a plan to collaborate with the national coordinator (Component A) to assist and monitor participating sites' IRB requests/approvals for participation in the longitudinal database.
• Demonstrate access to or describe a plan for data transfer to previously-created (established) longitudinal dataset
• Describe approach to develop a protocol for a quality control/quality assurance process periodically to improve the quality and reliability of the data.
• Describe the process for conducting a comprehensive review of the longitudinal dataset by the end of the project period to assess data quality.
• Describe the plan to collaborate with clinicians and researchers to conduct analyses using

the longitudinal datasets.
• Describe willingness to collaborate with the PI(s) of Component A and CDC representatives to implement guidelines and processes for data analysis and publications, which should include, but are not limited to:

o assuring and expediting orderly and timely presentation to the scientific community of all pertinent data emerging from the analyses of the longitudinal database;
o promoting accurate and scientifically sound presentations and papers involving the longitudinal database;
o promoting collaboration among clinicians and researchers participating in the longitudinal database and assuring that all participating sites have the opportunity to be involved in data analysis and the preparation of presentations and publications;
o assuring that press releases, presentations, and publications related to the longitudinal database are accurate and objective, and do not compromise the collaborative study and the acceptance of its results;
o establishing guidelines for authorship, acknowledgments, and funding citations for any presentations and publications based on the longitudinal database.

• Describe willingness to collaborate with the national coordinator (Component A) and other participating clinicians and researchers in order to conduct analyses that can address important clinical care and public health research questions. The goal is to deliver essential information that health care and allied professionals could use in providing better care and improving health outcomes and quality of life across the lifespan.
Describe willingness to collaborate with CDC to implement an evaluation plan. The evaluation plan may include, but is not limited to, assessment of 1) logistics of data collection; 2) documentation of enrollment and non-enrollment; 3) data quality and data preparation for analyses; and 4) the utility of the information gathered to answer clinical care and public health research questions 5) project outcomes.
• Describe a sustainability plan for activities specified under Component B after this one-year project period ends.

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 publicly 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 FOA must be followed. For this specific FOA, 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 35 pages for all appendices.

8. Format for Attachments

Designed to maximize system-conducted validations, multiple separate attachments are required for a complete application. When the application is received by the agency, all submitted forms and all separate attachments are combined into a single document that is used by peer reviewersand 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 (Part I, Section 2) (http://grants.nih.gov/ grants/funding/424/ SF424_RR_Guide_General_VerC.pdf).

9. Submission Dates & Times

Part I. Overview Information contains information about Key Dates. Applicants are encouraged to submit in advance of the deadline to ensure they have time to make any application corrections that might be necessary for successful submission.
Organizations must submit applications via Grants.gov (https://www.grants.gov), the online portal to find and apply for grants across all Federal agencies. The eRA Commons systems retrieve the application from Grants.gov and check the application against CDC business rules. If no errors are found, the application will be assembled in the eRA Commons for viewing by the applicant before moving on for further CDC processing.
If errors are found, the applicant will be notified in the eRA Commons. They must make required changes to the local copy of their application and submit again through Grants.gov.
Applicants are responsible for viewing their application in the eRA Commons to ensure accurate and successful submission.

Once you can see your application in the Commons, be sure to review it carefully as this is what the reviewer will see. Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (http:// grants.nih. gov/grants /guide/url_redirect .htm? id=11123).
Information on the submission process is provided in the SF424 (R&R) Application Guide.
Note: HHS/CDC grant submission procedures do not provide a period of time beyond the grant application due date 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). The application package is not complete until it has passed the Grants.gov/eRA Commons validation process. This process and email notifications of receipt, validation or rejection may take two (2) business days.
Applicants are strongly encouraged to allocate additional time prior to the submission deadline to submit their applications and to correct errors identified in the validation process. Applicants are encouraged also to check the status of their application submission to determine if the application packages are complete and error-free. Applicants who encounter system errors when submitting their applications must attempt to resolve them by contacting the Grants.gov Contact Center (1-800-518-4726; support@grants.gov). If the system errors cannot be resolved, applicants must contact TIMS at 770-488-2700; ogstims@cdc.gov for guidance at least 3 calendar days before the deadline date.
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. This validation process may take as long as two (2) business days. A third and final e-mail message is generated once the applicant's application package has passed validation and the grantor has confirmed receipt of the application.

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

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

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

2. Check his/her emails from both Grants.gov and eRA Commons for rejection notices.

    a. If the deadline has passed, he/she should email the Grant Management Specialist listed in the NOFO (ogstims@cdc.gov) explaining why the submission failed. b. If there is time before the deadline, he/she should correct the problem(s) and resubmit as soon as possible.

Due Date for Applications: **02/20/2020**

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

10. Funding Restrictions

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

11. Other Submission Requirements and Information

Application Submission

Applications must be submitted electronically following the instructions described in the SF 424 (R&R) Application Guide. **PAPER APPLICATIONS WILL NOT BE ACCEPTED**.
Applicants must complete all required registrations before the application due date.
Section III.6 "Required Registrations" contains information about registration.
For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically (http://grants.nih.gov/grants/guide /url_ redirect.htm? id=11144).

Important reminders: All PD/PIs must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF 424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to CDC.

The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management (SAM). Additional information may be found in the SF424 (R&R) Application Guide.

If the applicant has an FWA number, enter the 8-digit number. Do not enter the letters "FWA" before the number. If a Project/Performance Site is engaged in research involving human subjects, the applicant organization is responsible for ensuring that the Project/Performance Site operates under and appropriate Federal Wide Assurance for the protection of human subjects and complies with 45 CFR Part 46 and other CDC human subject related policies described in Part II of the SF 424 (R&R) Application Guide and in

the HHS Grants Policy Statement.
See more resources to avoid common errors and submitting, tracking, and viewing applications: http:// grants.nih. gov/grants/ Electronic Receipt /avoiding _errors.htm or http :// grants. nih.gov/grants/ Electronic Receipt/submit _app.htm
Upon receipt, applications will be evaluated for completeness by the CDC Office of Grants Services (OGS) and responsiveness by OGS and the Center, Institute or Office of the CDC. Applications that are incomplete and/or nonresponsive will not be reviewed.

Section V. Application Review Information

1. Criteria

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

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

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

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?

Components A and B:

- Does the project address an important problem related to the health and wellbeing of people with FXS?
- What is the potential impact of this work on the health and wellbeing of the population living with FXS?
- How will this work be influential in the fragile X clinical and research communities?

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?

Component A

- Does the PI have a record of research which has advanced the field of FXS clinical care or public health research?
- Has the applicant demonstrated a track record of working with multiple FXS specialty clinics?
- Is the applicant's past performance well suited to the project?
- Has the applicant demonstrated the willingness and ability to actively participate in project activities, collaborate with recipient of Component B funding, and assume an active role in the Steering Committee that is intended to encourage collaboration across components of this supplement and provide the necessary expertise and oversight to ensure successful completion of Components A and B?

Component B:

- Does the PI have a record of participating in research which has advanced the field of FXS clinical care or public health research?
- Has the applicant demonstrated a track record of working with multiple FXS specialty clinics?
- Is the applicant's past performance well suited to the project?
- Has the applicant demonstrated a track record of working with large databases and handling data from multi-site research projects?
- Has the applicant demonstrated the willingness and ability to actively participate in project activities, collaborate with recipient of Component A funding, and assume an active role in the Steering Committee that is intended to encourage collaboration across components of this supplement and provide the necessary expertise and oversight to ensure successful completion of Components A and B?

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?

Components A and B:

Does the project have the potential to improve the care of people affected by FXS?
Does the application seek to inform current research or clinical practice by contributing to the collection and analysis of longitudinal data?

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?

Component A:

• Has the applicant demonstrated an effective plan to maintain and expand the FORWARD longitudinal database?
• Is the plan sufficient to ensure the collection of one additional follow-up data point on at least 100 individuals with fragile X syndrome and new data on at least 90 new participants?
• Has the applicant provided a detailed plan for overseeing a national coordinator that can provide technical assistance to the clinics?
• Does the national coordinator have experience coordinating multi-site data collection?
• 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)?

Component B:

• Has the applicant demonstrated a sufficient plan to continue receiving, processing, securing, managing and analyzing data?
• Has the applicant demonstrated a plan to provide at least one FORWARD longitudinal dataset to be used for analyses?
• Has the applicant demonstrated a detailed and feasible plan to continue evaluating data quality, documenting findings from, and addressing issues found in the evaluation?
• Has the applicant provided a detailed staff and resources plan, including a description of the staff commitments and necessary expertise of staff to operate as the Data Coordinating Center?
• Has the participant demonstrated access to previously-created longitudinal dataset or provided a plan for data transfer of previously-created longitudinal dataset?

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?

Components A and B

• Has the applicant demonstrated the ability to work with multiple FXS specialty clinics to support data collection for the longitudinal database? Are there letters of support from the FXS specialty clinics?
• 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?
• Has the applicant demonstrated a plan to share results with the fragile X clinical and research communities?

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 and the policy on the Inclusion of Persons Under 21 in Research (https://www.cdc.gov/maso/Policy/policy496.pdf).

Vertebrate Animals The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Verterbrae Animal Section (https://grants.nih.gov/grants/olaw/VAChecklist.pdf).

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

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

concern, visit the U.S. Government Science, Safety, Security (S3) website at: http://www.phe.gov/s3/dualuse. Tools and guidance for assessing DURC potential may be found at: http://www.phe.gov/s3/dualuse/Pages/companion-guide.aspx.

3. Additional Review Considerations

As applicable for the project proposed, reviewers will consider each of the following items, but *will not give scores* for these items, and should not consider them in providing an overall impact/priority score.
HHS/CDC will assess the reasonableness of the data sharing plan. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The presence of a data sharing plan will be part of the terms and conditions of the award. The funding organization will be responsible for monitoring the data sharing policy.

Data sharing agreement

Awardees will retain custody of and have primary rights to their data developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies. The collaborative protocol and governance policies will call for the participating sites to submit de-identified data for the longitudinal database to the Data Coordinating Center; the submission of copies of the de-identified datasets to CDC; procedures for data analysis, reporting and publication; and procedures to protect and ensure the privacy of medical and genetic data (if any) and records of individuals. The study will be expected to put all study materials and procedures manuals in the public domain and/or make them available to qualified investigators. Awardees are encouraged to publish and to publicly release and disseminate results, data and other products of the study, concordant with the study protocol and governance and the approved plan for making data and materials available to the scientific community.

Resource Sharing Plans 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: http://www.cdc.gov/grants/additionalrequirements/index.html. Investigators responding to this funding opportunity should include a plan on sharing research resources and data.

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

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 decisions:

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

5. Anticipated Announcement and Award Dates

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

Section VI. Award Administration Information

1.Cooperative Agreement Terms and Conditions of Award

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:

- Complying with the responsibilities for Extramural Investigators as described in the Policy on Public Health Research and Nonresearch Data Management and Access http:/intranet.cdc.gov/od/oads/spa/dma/index.html
- Component A primary responsibilities:
    - o Providing oversight of all management, administrative, and scientific aspects of the project in collaboration with the fragile X specialty clinics.
    - o Providing oversight of the national coordinator.
    - o Serving on an overarching Steering Committee for FORWARD. Members of the Steering Committee must include PIs from Components A and B and CDC representative(s). The Steering Committee may include non-voting members and PIs for current recipients of DD15-003.
    - o Collaborating with the Data Coordinating Center (Component B) to obtain and maintain the appropriate Institutional Review Board approvals for all institutions or

individuals participating in the research project and providing this documentation to CDC as required.
o Ensuring timely responses to all quality assurance/quality control (QA/QC) queries.
o Working collaboratively with CDC to revise, as needed, the research protocol, research agenda, and data sharing agreement that details data use, access, sharing of de-identified data with CDC collaborators, publication plan, and review of analyses.
o Adhering to established Publication and Data Sharing Guidelines.
o Providing accurate and timely reports, per guidance in the "Reporting" section below.

• Component B primary responsibilities:

o Providing oversight of all management, administrative, and scientific aspects of the project in collaboration with Component A.
o As needed, collaborating with Component A to provide training to fragile X specialty clinics on data collection and data quality assurance.
o Maintaining data quality, promoting efficient data collection, and supporting clinics to send de-identified data to the data management and analysis center.
o Collaborating with the national coordinator (Component A) to obtain and maintain the appropriate Institutional Review Board approvals for all institutions or individuals participating in the research project; and provide this documentation to CDC as required.
o Ensuring a de-identified dataset is shared with CDC for this 1-year project period.
o Serving on an overarching Steering Committee for FORWARD. Members of the Steering Committee must include PIs, from Components A and B and CDC representative (s). The Steering Committee may include non-voting members and PIs for current recipients of DD15-003.
o Participating in other committees and workgroups that work across components A, B.
o Working collaboratively with CDC to revise, as needed, the research protocol, research agenda, and data sharing agreement that details data use, access, sharing of de-identified data with CDC collaborators, publication plan, and review of analyses.
o Adhering to established Publication and Data Sharing Guidelines.
o Providing accurate and timely reports, per guidance in the "Reporting" section below.

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. 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 http://intranet.cdc.gov/od/oads/spa/dma/index.html
• An HHS/CDC Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

There are two separate CDC scientific roles – Scientific Collaborator (SC) and Scientific Program Official (SPO). In this cooperative agreement, a NCBDDD SC is an equal partner with

scientific and programmatic involvement during the conduct of the project through technical assistance, advice, and coordination.
The SC will:

- Provide expertise and guidance on the project.
- Support the recipients' activities in data collection, management, and analysis.
- Assist in the analyses, interpretation, and reporting of findings in the literature.
- Serve as one of the CDC representatives on the overarching Steering Committee intended to provide guidance and expertise with regard to successful completion of Components A and B. Members of the Steering Committee must include PIs from Components A and B and CDC representative(s). The Steering Committee may include non-voting members and PIs for current recipients of DD15-003.
- Participate in the QA/QC activities.
- Collaborate with the recipient to implement the evaluation plan.

Additionally, an HHS/CDC Project Officer or other HHS/CDC staff will provide day-to-day programmatic, administrative, and fiscal management in support of the project as defined above.

An HHS/CDC agency Program Official will be responsible for the normal scientific and programmatic stewardship of the award.
The SPO 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
- Assure 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:

- Collaborate with leadership from each of the Components, CDC representatives, and other individuals and organizations as applicable.
- Participate in a Steering Committee assembled to encourage collaboration across components of this supplement and to provide the necessary expertise and oversight to ensure successful completion of the activities contemplated in this supplement.
- Components A and B. Members of the Steering Committee will include PIs, or co-PIs, from each awarded site from Components A and B and CDC staff. The Steering Committee may consider adding non-voting liaisons from patient-oriented organizations, including but not limited to, the National Fragile X Foundation and FRAXA Research Foundation. Additional non-voting members must be unanimously approved by members of the designated Steering Committee described above The Steering Committee may include PIs for current recipients of DD15-003.

    a. Each year the Chair of the Steering Committee shall be elected by the members of the Steering Committee. The Chair must be one of the PIs for Components A or B. The PI shall serve as Chair for at least six months.
    b. The Steering Committee should meet at least monthly by phone for the duration of

the Cooperative Agreement and may be required to meet more frequently as needed.
c. The Steering Committee shall meet in-person at least once for the duration of the Cooperative Agreement.

• Recipients of Components A and B will be expected to communicate regularly with one another and the CDC. This could include, but is not limited to, monthly calls, in-person meetings, webinars, and email communication.
• Recipients of Components A and B shall coordinate one in-person grantee meeting.
• Recipients of Components A and B shall work together to conduct analyses and develop presentations and publications for the scientific and lay audiences.
• Collaborate with clinicians and researchers from the sites participating in the longitudinal database, the PIs of each Component and CDC representatives to identify important clinical care and public health research questions and utilize data from the longitudinal database to address them.
• Collaborate with the PIs of Component A and B and CDC representatives to establish and implement guidelines and processes for data analysis and publications.

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

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CDC Technical Information Management Section (TIMS)

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Awards are made under the authorization of Sections 301 and 317 (C) of the Public Health Service Act as amended, and under Federal Regulations (42 U.S.C., Sections 241 and 247b-4) as amended.

Appendix A. Questions from Potential Applicants and CDC Responses

Question: (1) Why is the focus on 85% patient follow-up for Component C and not Component A? What about patients that are not enrolled in FORWARD, and don't come to the clinic often? Does the patient count as previously enrolled longitudinal database? Do we document a plan for non-current patient that are not being seen frequently? How does the CDC intend to handle this or be defined?

Answer: (1) Anyone currently enrolled in FORWARD will qualify. In Section IV. "Application and Submission Information", under "5. PHS 398 Research Plan Component" on page 20 of the FOA under Component C, it states how to handle returning patients. It is up to the applicant to describe a plan to identify patients coming into clinics.

Question: (2) Does [criteria from Question 1] apply to only Component C?

Answer: (2) Yes, it only applies to Component C.

Question: (3) Does Component C have fewer patients? Why doesn't Component A address

minority and underserved populations?

Answer: (3) Component C is specifically funding the inclusion of minorities and underserved populations. However, the overall purpose of the RFA addresses the inclusion of minorities and underserved populations, so potential applicants are welcomed to address this in Component A if the applicant thinks it contributes to the best way to meet the purpose and objectives of the RFA.

Question: **(4)** Describe the difference in the number of patients between Component A and Component C? Can there be any overlap between the two budgets?

Answer: (4) Each component has an individual budget; each activity has its own specific budget. Each component is submitted as a separate application. The applications will be reviewed and considered separately.

Question: (5) What website will be used to submit the applications?

Answer: (5) Each applicant should register and submit their application through www.grants.gov. Principal investigators should submit their information through the ERA Commons system.

Question: (6) What are the roles of the Principal Investigators and Co- Investigators?

Answer: (6) Only 1 Principal Investigator (PI) is needed per application. Only one PI can be the primary contact for each application. Component C has up to 3 awards, therefore there will be up to 3 individual PIs - different institutions will have a different Principal Investigator for each award. If applying for more than one component, applicants must designate a primary PI for each component, as the applications for each component are submitted separately. This can be the same person or different people.

Question: (7) Will there be a requirement to get all the applicants to agree to certain outcome measurements? Outside of the CDC will there be a way to form a core group that will agree to certain outcome measures?

Answer: (7) Applicants can propose any approach that they feel will best be able to meet the objectives as outline in the RFA.

Question: (8) Do you have any set requirements for Component C regarding funding applicants that focus on minority and underserved populations versus outcome measures?

Answer: (8) Applicants are encouraged to propose a project focus that they feel best meets the requirements and intent of the RFA. This is noted in Section V. “Application Review Information”, Part 4. “Review and Selection Process” on page 30 of the FOA which states “.the following will be considered in making funding decisions … Component C: Diversity of project focus (outcome measures and targeting minority or underserved)”.

Question: (9) Do we have to use an outcome measurement from the list of multiple options on the document?

Answer: (9) No, applicants can choose to use a measurement not on the list. In Section IV. “Application and Submission Information”, Part “5. PHS 398 Research Plan Component”, in the “Research Plan” section of the FOA on page 21, under “Component C” it states the following: “If choosing a measure not listed below describe the measure, previous validation

studies (if any), and provide justification for the selection."

Question: (10) Could you provide a description of the compensation plan for participating in a longitudinal database? If a clinic is compensated for one component, can the clinic also be compensated in a different component?

Answer: (10) In your application, if compensation is part of the plan, the application needs to describe the plan for compensation. Entities cannot be compensated twice for the same activity. Please refer to Section IV. "Application and Submission Information", Part "5. PHS 398 Research Plan Component", in the "Research Plan" section of the FOA on page 18, under "Component A" which states "If proposing clinic compensation for participation in the longitudinal database, describe the compensation plan ONLY for clinics not compensated through Component C."

Question: (11) Can you divide a clinic into two sub-clinics?

Answer: (11) The RFA does not specify how to address this. This method can be proposed by an applicant if they feel it is the strongest approach to meeting the goals and objectives of the RFA.

Question: (12) The RFA does not specify that individual level data be held at Component B institution only. May individual level data be released to National Coordinator and staff for purposes of study coordination (checking on clinic entries and assisting with follow-up as needed by direct contact) and simple data examinations (not analyses for papers) if clinic IRB and clinic director approval is met?

Answer: (12) Under the "Data sharing agreement" described in Section V. "Application Review Information" Part "3. Additional Review Considerations" of the FOA (page 29), it states the "awardee will retain custody of and have primary rights to their data developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies."

The awardee of Component B will be responsible for data management and data security. Applicants for Component B have been asked to "describe the processes for protecting human subjects, including protecting personal identifying information." How individual level data are collected, managed, stored, and if applicable shared, is for the applicant to describe in their application, as this all falls under protecting human subjects (see Section IV. "Application and Submission Information", Part "5. PHS 398 Research Plan Component", under "Research Plan", under "Component B" of FOA pages 19-20).

Question: (13) Must applicants for Component C be clinic directors or clinic coordinators, or can they be affiliated with a clinic in other ways?

Answer: (13) It is up to the applicant to propose who the PI and affiliated personnel will be. The applicant must also meet the special eligibility criteria described in Section III. "Eligibility Information", Part 3. "Special Eligibility Requirements" on page 13 of the FOA. Per the FOA, under Section V. "Application Review Information", under "Investigator(s)" on page 25, the general review criteria for Investigators states "are the PD/PIs, collaborators, and other researchers well suited to the project?"; "Have they demonstrated an ongoing record of accomplishments that have advance their field(s)?"

Specific to Component C (page 26) there are five additional bulleted review criteria under

"Investigator(s)" that will be considered. The PI needs to have the necessary expertise and oversight to ensure successful completion of the research plan proposed (the applicant's research plan should respond to what is outlined in Section IV. "Application and Submission Information", Part "5. PHS 398 Research Plan Component" under "Component C – Enhanced Participation of Fragile X Specialty Clinics" on pages 20-21 of the FOA). The PI must also have expertise and oversight capability to participate on a Steering Committee that encourages collaboration across components of the FOA ("Section V.", "Investigator(s)", "Component C", page 26).

Question: (14) What kind of sustainability plan (page 19) is expected – any templates from other CDC grants that applicants can refer to?

Answer: (14) This is for the applicant to propose. Other templates or models (properly referenced) that the applicant identifies can be used to inform the plan.

Question: (15) There was no mention of in-person meetings for the participating clinics – only travel by the National Coordinator to conduct site visits to assist with trouble-shooting. Given that the clinics are all over the country, these meetings assist in coordinating data collection interpretation and fielding concerns with trouble-shooting. Can the budget of A or Cs be used for this?

Answer: (15) The applicant can propose a research plan, including meetings and travel, that includes activities that they think will best address the purpose of the FOA (on pages 5-6) the objectives and outcomes (on pages 7-10 in Section I. "Funding Opportunity Description", 2. "Approach") and the Research Plan (on pages 17-21 in Section IV. "Application and Submission Information", under "5. PHS 398 Research Plan Component").