



Centers for Disease Control and Prevention

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

Study to Explore Early Development (SEED) Follow up Studies

RFA-DD-21-001

Application Due Date: 11/10/2020

Study to Explore Early Development (SEED) Follow up Studies
RFA-DD-21-001
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Part 1. Overview Information

Participating Organization(s)

Centers for Disease Control and Prevention

Components of Participating Organizations

National Center on Birth Defects and Developmental Disabilities

Notice of Funding Opportunity (NOFO) Title

Study to Explore Early Development (SEED) Follow up Studies

Activity Code

U01

Amendment 2 (10/22/20):

Section I, #2. Approach, Requirements for Component A, item #4.

- For Component A, two LOIs will be required in Y2. The NOFO has been updated to remove the conflicting statement of requirements for Y2. This is in reference to Q12 in Appendix C.

Section I, #2. Approach, Requirements for Component A, item #11.

- For Component A, participant eligibility criteria for inclusion in the follow-up surveys has been updated. Former SEED participants are eligible if they received a final study classification of ASD, DD or POP and the mother or primary caregiver consented to future follow-up. This is in reference to Q3 in Appendix C.

Section I, #2. Approach, Introduction to Requirements for Component B

- For Component B, participant eligibility requirements have been updated. Former SEED participants are eligible if they (1) received a final class of ASD or DD in SEED 1,2, or 3; (2) completed the clinic visit, including the Mullen Scales of Early Learning, during SEED 1,2 or 3; and (3) completed the first follow-up survey in Component A. This is in reference to Q3 in Appendix C.

Section III, Eligibility Information, #3. Additional information on Eligibility

- The entities previously funded by CDC to collect data for SEED 1,2, or 3 have been updated to include the Regents of the University of Colorado. This is in reference to Q31 in Appendix C.

Section VIII. Other Information

- Applicant questions and CDC responses have been added to Appendix C. Additional Q&As have been added to Appendix C (Questions from Potential Applicants and CDC Responses).

Amendment 1 (9/18/20): Added informational webinar for applicants that will be held on October 2, 2020, from 11:00am-12:30pm. For details, see Part 1, Executive Summary under

Special Date(s).

Notice of Funding Opportunity Type

New

Agency Notice of Funding Opportunity Number

RFA-DD-21-001

Assistance Listings (CFDA) Number(s)

93.073

Category of Funding Activity:

Health

NOFO Purpose

The purpose of this NOFO is to gain knowledge about autism spectrum disorder (ASD), including risk factors for ASD and the expression of ASD, from childhood through early adulthood to improve the health and functioning of individuals with ASD as they mature. This will be accomplished through five funding components (described in the Executive Summary of this NOFO). Together, these five funding components will support 1) analysis of existing data and biospecimens from preschool aged children and their families who participated in the CDC funded study known as the Study to Explore Early Development (SEED), a multi-phase, multi-site, case-control study of children identified at age 2-5 years with ASD, other developmental disabilities (DD), and from the general population (POP); and 2) longitudinal follow-up surveys and research on previous SEED participants to obtain information through early adulthood on their health and functioning, service use and needs, and the impact of ASD on their families.

Key Dates

Publication Date:

To receive notification of any changes to RFA-DD-21-001, 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:

10/05/2020

Application Due Date:

11/10/2020

On-time submission requires that electronic applications be error-free and made available to CDC for processing from the NIH eRA system on or before the deadline date. Applications must be submitted to and validated successfully by Grants.gov no later than 5:00 PM U.S. Eastern Time. Applications must be submitted using the Application Submission System & Interface for Submission Tracking (ASSIST) module which is a web-based service used for the preparation and submission of grant applications to CDC through Grants.gov. ASSIST provides the ability for applicants to prepare their applications online, and offers the applicant additional capabilities including the ability to preview the application image, validate the application against required business rules, and prepopulate data from an applicant organization's records, therefore identifying issues earlier in the application submission process.

Note: HHS/CDC grant submission procedures do not provide a grace period beyond the application due date time to correct any error or warning notices of noncompliance with application instructions that are identified by Grants.gov or eRA systems (i.e., error correction window).

Scientific Merit Review: 01/13/2021

Secondary Review: 02/22/2021

Estimated Start Date: 07/01/2021

Expiration Date: 11/11/2020

Due Dates for E.O. 12372: Executive Order 12372 does not apply to this program.

Required Application Instructions

****ELECTRONIC APPLICATION SUBMISSION VIA ASSIST IS PREFERRED****

It is recommended that applicants use ASSIST for the electronic preparation and submission of applications through Grants.gov to CDC. ASSIST is an alternative method to prepare and submit applications, and provides many features to facilitate the application submission process which improves data quality (e.g., pre-population of organization data, pre-submission validation of business rules, and preview of the application image used for review). Use of the Grants.gov downloadable Adobe application packages and submission process will still be supported.

It is critical that applicants follow the instructions in the [SF 424 \(R&R\) Application Guide](#) except where instructed to do otherwise in this NOFO. Conformance to all requirements (both in the Application Guide and the NOFO) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Note: The Research Strategy component of the Research Plan is limited to 25 pages.

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

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

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

Executive Summary

- **Purpose.** The purpose of this NOFO is to gain knowledge about autism spectrum disorder (ASD), including risk factors for ASD and the expression of ASD, from childhood through early adulthood, and to obtain information that can be used to improve the health and functioning of individuals with ASD as they mature. This will be completed through

1) analysis of existing data and biospecimens from preschool-aged children and their families who participated in the CDC funded study known as the Study to Explore Early Development (SEED), a multi-phase, multi-site, case-control study of children identified at age 2-5 years with ASD, other developmental disabilities (DD), and from the general population (POP); and 2) longitudinal follow-up of and research on previous SEED participants to obtain information through early adulthood on their health and functioning, service use and needs, and the impact of ASD on their families.

These activities will be accomplished through five components (A-E):

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants To conduct analyses of existing SEED data and follow-up surveys of participants from SEED Phases 1, 2, and 3 (referred to as SEED 1-3) to

1. Address current research gaps, and publish findings related to risk factors for ASD and the characteristics and needs of children with ASD; and
2. Support the implementation of follow-up surveys in collaboration with CDC from an existing list of SEED participants in SEED 1-3.

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants To conduct follow-up assessments of intellectual abilities on a subset of children and adolescents (aged ≥ 8 years), who were initially identified as having ASD or another DD in SEED 1-3 and who completed the follow-up surveys implemented through Component A of this NOFO. To be funded for Component B, applicants must apply and be funded for Component A.

Component C: Maternal Auto-Antibody Testing To conduct assays of maternal autoantibodies reactive to proteins in the fetal brain using stored SEED 1 and 2 samples and to conduct analyses of the association between these maternal autoantibodies and ASD. To be funded for Component C, applicants must apply and be funded for Component A.

Component D: Genetic Analyses To identify analytic priorities for generating and analyzing SEED genetic data; to develop and implement methods for combining existing SEED 1 genetic data and newly generated SEED 2 and 3 genetic data for use by SEED investigators and contribution to data repositories; and to support SEED investigators conducting analyses to increase understanding of the genetic risk factors for ASD and their interaction with environmental risk factors. To be funded for Component D, applicants must apply and be funded for Component A.

Component E: Biorepository To maintain a repository of biospecimens previously collected from SEED 1-3 participants. To be funded for Component E, applicants must apply and be funded for Component A.

Applicants should clearly indicate the components for which they are applying and should include, at the beginning of the title, the respective component under which the application should be considered (i.e., Component A, B, C, D, and/or E). A separate application is required for each component.

- **Mechanism of Support.** Cooperative Agreement
- **Funds Available and Anticipated Number of Awards.** The estimated total funding (direct and indirect) for the period of performance is \$16,370,000 to support up to six

anticipated awards for Component A, up to two awards for Component B, one award for Component C, one award for Component D, and one award for Component E, for a total of up to 11 awards for the five components.

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants

Period of Performance: 5 years (7/1/2021 - 6/30/2026)

Anticipated Number of Awards: Up to six

Ceiling: \$750,000 (direct and indirect costs) (Note: the ceiling assumes the awardee will collaborate with two or more former SEED sites to contact participants and have a minimum of 2,400 eligible participants in their sample pool.)

Floor: \$230,000 (direct and indirect costs)

Estimated Average Award (Note: this average award is based on an eligible sample of 800 participants with the funding adjusted up or down based on the number of participants):

- Budget Year 1: \$425,000 (direct and indirect costs)
- Budget Years 2-5: \$405,000 (direct and indirect costs)

Estimated Total Funding: \$12,270,000 (direct and indirect costs)

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

Period of Performance: 4 years (7/1/2021 - 6/30/2025)

Anticipated Number of Awards: Up to two

Ceiling: \$20,000 (direct and indirect costs) (Year 1 only)

Floor: \$0

Estimated Average Award:

- Budget Year 1: \$20,000 (direct and indirect costs)
- Budget Years 2-4: \$160,000 (direct and indirect costs)

Estimated Total Funding: \$1,000,000 (direct and indirect costs)

Component C: Maternal Auto-Antibody Testing

Period of Performance: 3 years (7/1/2021 - 6/30/2024)

Anticipated Number of Awards: One

Ceiling: \$200,000 (direct and indirect costs)

Floor: \$0

Estimated Average Award for First Year: \$200,000 (direct and indirect costs)

Estimated Total Funding: \$600,000 (direct and indirect costs)

Component D: Genetic Analyses

Period of Performance: 5 years (7/1/2021 - 6/30/2026)

Anticipated Number of Awards: One

Ceiling: \$540,000 (direct and indirect costs) (Note: the ceiling assumes the awardee will provide secure access to high-capacity computing servers that meet Federal standards for security and confidentiality for approved SEED investigators. Applicants who are not able to provide access to high-capacity computing servers for approved investigators will receive an award closer to the average of \$450,000.)

Floor: \$0

Estimated Average Award for First Year: \$450,000 (direct and indirect costs)

Estimated Total Funding: \$2,250,000 (direct and indirect costs)

Component E: Biorepository

Period of Performance: 5 years (7/1/2021 - 6/30/2026)

Anticipated Number of Awards: One

Ceiling: \$50,000 (direct and indirect costs)

Floor: \$0

Estimated Average Award for First Year: \$50,000 (direct and indirect costs)

Estimated Total Funding: \$250,000 (direct and indirect costs)

Awards issued under this NOFO are contingent upon availability of funds and a sufficient number of meritorious applications. Because the nature and scope of the proposed research will vary from application to application, it is also anticipated that the amount of each award may also vary. The total amount awarded, and the number of awards, will depend upon the number, quality, duration and cost of the applications received.

- **Budget and Project Period.** The estimated total funding (direct and indirect) for the first budget period, 7/1/2021 - 6/30/2022, is \$3,290,000. The estimated total funding (direct and indirect) for the entire 5-year performance period (7/1/2021 - 6/30/2026), including all components, is \$16,370,000.
- **Application Research Strategy Length.** Page limits for the Research Strategy are clearly specified in [Section IV Application and Submission Information](#) of this announcement.
- **Eligible Institutions/Organizations.** Institutions/organizations listed in [Section III, 1.A.](#) 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 through their organization.
- **Number of PDs/PIs.** Applications may include more than one PI; however, the first PI listed on the application will be the contact PI for all correspondence. Any additional PIs are permitted but would be referred to as Co-PIs.

- **Number of Applications.** Only one application per institution (normally identified by having a unique DUNS number) is allowed per component for this NOFO. All eligible applicants for Component A can also apply for Components B, C, D, and/or E. To be funded for components B, C, D, and/or E, eligible applicants must apply for and be funded for Component A. Separate applications are required for each component.
- **Application Type.** New.
- **Special Date(s).** Informational webinar for applicants will be held on October 2, 2020, from 11:00am-12:30pm EST. Attendees are encouraged to submit questions in advance to ResearchNOFO@cdc.gov.
 - Join ZoomGov Meeting
 - <https://cdc.zoomgov.com/j/1612051963?pwd=MkR1UkQ5MFVhRng5S0RZVTIHZkF6QT09>. Meeting ID: 161 205 1963, Passcode: yT\$RKLf3
 - Dial by your location: +1 669 254 5252 US (San Jose), +1 646 828 7666 US (New York), Meeting ID: 161 205 1963, Passcode: 42481162
- **Application Materials.** See [Section IV.1](#) for application materials. Please note that Form E is to be used when downloading the application package. <http://grants.nih.gov/grants/how-to-apply-application-guide/forms-d/general-forms-d.pdf%20>

Part 2. Full Text

Section I. Funding Opportunity Description

Statutory Authority

Sections 301(a) [42 U.S.C. Section 241(a)] and 317C of the Public Health Service Act [42 U.S.C. Section 247b-4)], as amended. Further authorization is provided under Pub. Law No. 106-310, Public Health Service Act; Pub. Law No. 109-416, Combating Autism Act of 2006; Public Law No. 113-157, Autism CARES Act of 2014; and Public Law No. 116-60, Autism CARES Act of 2019.

1. Background and Purpose

Background

In 2016, an estimated 1 in 54 children 8 years of age living in 11 communities across the United States had autism spectrum disorder (ASD) [1], a developmental disability that can cause significant social, communication, and behavior challenges. Total annual cost associated with ASD have been estimated between \$11.5-\$60.9 billion (2011 US dollars) [2], yet major gaps in knowledge remain about risk factors for ASD, and associated challenges and needs for persons with ASD and their families [3]. Most research on ASD has focused on children, yet ASD is considered a lifelong condition, and although an estimated 70,000 to 111,000 youth with ASD turn 18 years of age annually [4], little is known about the transition to adolescence and adulthood for persons with ASD [5]. Despite the call to address transition and lifespan issues in the Autism CARES Acts of 2014 and 2019, only 2% of ASD funding from 2008-2018 was spent on lifespan issues [6]. To address these gaps, this NOFO will assess risk factors for and characteristics of preschool age children with ASD using previously collected data and biospecimens from the Study to Explore Early Development, Phases 1, 2, and 3 (SEED 1-3) and

will conduct longitudinal follow-up studies of SEED 1-3 participants at older ages.

SEED 1-3 (also known as SEED) is a multi-phase, multi-site, case-control study comparing children with ASD, identified at ages 2-5 years, to children with other non-ASD developmental disabilities (DD), and from the general population (POP). SEED was established to address the Children's Health Act of 2000 which mandated CDC to conduct ASD surveillance and implement research programs to address the number, incidence, and causes of ASD and related developmental disabilities. Under this legislation, CDC's National Center on Birth Defects and Developmental Disabilities funded a network of five Centers for Autism and Developmental Disabilities Research and Epidemiology, that developed and implemented SEED. Through the three phases (2006-2011, 2011-2016, and 2016-2021), SEED was implemented in limited geographic areas within portions of eight states (California, Colorado, Georgia, Maryland, Pennsylvania, and North Carolina, during SEED 1 and 2; and in Colorado, Georgia, Maryland, Missouri, North Carolina, and Wisconsin, during SEED 3).

Across all three phases of SEED, the common scientific aims were to

1. Characterize the behavioral phenotypes and associated developmental, medical and behavioral conditions of ASD among preschool-aged children; and
2. Understand the genetic and environmental risk factors for ASD, with environmental factors focusing on infectious, immunological, hormonal, obstetric, gastrointestinal and socio-demographic features.

Comprehensive data collected through SEED includes study participant data (including information on pregnancy and early childhood exposures, services and treatments, maternal medical history, family socio-demographics, and child health and development), standardized functional assessments, and biospecimens. ASD status of children in the study is based on the results of comprehensive standardized evaluations [7].

While SEED 3 data collection is ongoing through mid-2021, analyses of data and biological specimens from SEED 1 and SEED 2 have increased our understanding of

1. Environmental risk factors for ASD (e.g., infectious, immunological, hormonal, obstetric, perinatal, and early childhood exposures) [8-23];
2. Genetic and epigenetic risk factors for ASD [24-26];
3. ASD phenotypes, co-occurring conditions, and health of children with ASD [27-35];
4. Safety considerations for children with ASD [36-39];
5. ASD screening, diagnosis, treatment, and use of services [40-44].

Yet, research gaps remain. With the completion of data collection in SEED 3, the large final sample size of the combined SEED 1-3 data set (including >6,000 children, of whom approximately 1,700 children with ASD will be included), will provide increased statistical power to explore research gaps such as those highlighted in the 2016-2017 Interagency Autism Coordinating Committee (IACC) Strategic Plan [6], and prioritized by major ASD advocacy organizations. Some of these gaps include differences in ASD characteristics and associated risk factors by sex or racial-ethnic groups; the association of maternal immune factors with ASD; and the interaction of genetics and the environment in their association with ASD. Research gaps related to associations of ASD with maternal immune and genetic risk factors are described in more detail below in sections titled *Maternal Immune Factors* and *Genetic Factors*.

Support through this NOFO is meant to help address these research gaps.

In addition to the research gaps summarized above and described in more detail below, the IACC Strategic Plan indicated more information is needed about the services and supports needed to maximize the quality of life for people on the autism spectrum, especially as individuals with ASD progress into adulthood.

Given the size of the original SEED birth cohorts and the wealth of baseline information collected, a follow-up study of participants can help us to better understand the developmental trajectory of children with ASD, their health outcomes and co-occurring conditions at older ages, and the associated early predictors of these outcomes, including intellectual abilities (described in more detail below in the section titled *Intellectual Abilities*). Additionally, because most SEED 1 participants will reach young adulthood (i.e., age 18 years) in years 2021-2026, data collected through Component A of this NOFO will provide an opportunity to assess changes in service access and utilization that may occur following high school exit. This period is particularly challenging for young adults with ASD who can experience poor outcomes across multiple domains (i.e., employment, education, social engagement, independent living, and access to health and mental health care services [45, 46]) in association with the loss of well-integrated school-based services [47, 48]. Hence, through surveying SEED 1 participants before and after their anticipated exit from high school, data collected through Component A of this NOFO could provide important information on the loss of services and emerging issues that can inform service delivery and programs on the supports needed to achieve greater independence.

Initial follow-up surveys of SEED participants at older ages must be conducted with the parents of children who previously participated in SEED because they provided consent for follow-up studies. However, many emerging issues surrounding the transition to adulthood among adolescents with ASD require self rather than parental report (e.g., self-reported symptoms of anxiety, depression, quality of life, social camouflaging, gender identity, sexuality, and relationships). Thus, data collected through Component A of this NOFO also provides the opportunity to obtain important self-reported measures of well-being among young adults with ASD.

Intellectual Abilities

Intellectual functioning is one of the strongest predictors of key outcomes among adolescents and young adults with ASD [49], yet previous studies suggest intellectual development is highly malleable and variable in early childhood [50-53]. As such, the intellectual abilities assessed in SEED 1-3, when participants were 2-5 years of age, may not be an accurate predictor of outcomes in adolescents and young adults with ASD. Moreover, parent report of overall intellectual ability is only moderately correlated with measured intelligence and may be underestimated by parents whose child exhibits greater ASD symptom severity [54, 55]. Assessing intellectual ability at later ages, when intellectual level is more stable, provides a more accurate measure of future intellectual performance [56-58]. This NOFO will allow for an assessment and potential correction for changes in intellectual ability as children with ASD age to account for potential error in alternative measures of intellectual function (e.g., parental self-report), in association with key outcomes. Because it is expected that some of the children classified as DD in SEED 1-3 will subsequently receive an ASD diagnosis by the time of follow-up [59], applicants to Component B of this NOFO will have the opportunity to assess

intellectual abilities of children in this group as well.

Recent evidence suggests that individuals with ASD with average to above average levels of intellectual functioning may still struggle with activities of daily living [60-63]. Yet, adults with special needs are often required to have an intellectual disability in order to qualify for services. Data collected in Component B of this NOFO will allow investigators to describe the gap between intellectual ability and daily living skills in adolescents with ASD to inform public policies on eligibility for services.

Maternal Immune Factors

Dysregulation of the maternal immune system during gestation has been associated with deleterious changes in neurodevelopment of children, and the study of the association of maternal immune factors with ASD is one of the original identified priorities for SEED. Although antibodies that recognize central nervous system antigens cannot cross the blood brain barrier in healthy adults, they can penetrate the fetal brain while it is still immature [64]. Recent research indicates maternal autoantibodies reactive to central nervous system proteins are associated with increased risk of ASD [64, 65]. Additionally, these antibodies are more common among women with autoimmune disorders, and also can be stimulated by immune activation from infection or chronic metabolic conditions in pregnancy (e.g., maternal obesity, gestational diabetes, and hypertensive disorders), all of which have been associated with ASD [64, 66, 67]. Moreover, among children with ASD, those whose mothers have reactive autoantibodies have higher rates of certain behavioral phenotypes (e.g., stereotypical behaviors, developmental regression, language deficits) than those whose mothers do not have reactive autoantibodies [64-66]. Thus, some speculate the presence of reactive maternal autoantibodies could account for a unique subtype of ASD [66]. Support through NOFO Component C will provide the ability to test for the presence of maternal autoantibodies reactive to fetal proteins involved in neurodevelopment in serum and plasma samples of SEED 1-2 participants. The detailed phenotypic data on children and pregnancy history data on mothers from SEED, along with data on maternal autoantibodies will allow investigators to better understand the associations between maternal immune factors and ASD.

Genetic Factors

The contribution of genetics to ASD is supported by its high heritability [68], yet there is also substantial evidence for environmental risk factors and gene by environment interactions [3, 69]. Research over the past decade has successfully identified a number of rare inherited and *de novo* gene variants conferring substantial risk for ASD [70-73]. Nonetheless, growing evidence suggests much of the risk for ASD and related neurodevelopmental and psychiatric disorders is attributable to the cumulative effects of multiple common variants, which in combination with environmental factors, can push individuals over a threshold for disease [70, 71, 74, 75]. However, it has been difficult to replicate studies identifying common variants related to ASD due to the relatively small effects of each variant and the need for larger sample sizes than available from existing studies [3, 71-73]. Similarly, most studies on gene by environment interactions related to ASD lack sufficient sample size and statistical power to account for multiple comparisons and variation in environmental exposures and data [3, 69].

Currently, SEED is the largest US-based study of ASD that has collected biospecimens and comprehensive developmental evaluations, along with detailed and standardized prenatal and early childhood environmental (non-genetic) exposure data; SEED thus offers an important

opportunity to examine genetic, environmental, and epigenetic risk factors for ASD in the same individuals. For SEED 1, single nucleotide polymorphism (SNP), copy number variation (CNV), and DNA methylation data were generated on ASD and general population control (POP) mothers and children, and were used to identify potential genetic and epigenetic correlates of ASD, including potential immune pathways and environmental exposures (i.e., smoking) associated with increased risk [24-26]. SEED 2-3 biospecimens are also available but, to date, no genetic or epigenetic data have been generated. Obtaining sufficient sample size and increased statistical power to estimate small effects from common genetic variants and environmental interactions will require the full set of SEED data and combining SEED data with other large studies [3, 69]. Support through Component D of this NOFO will provide investigators the opportunity for genetic analyses by providing SEED collaborators with the needed expertise in analytic techniques for merging multiple datasets generated on different genotyping platforms and adjusting for temporal differences [76]. Finally, support for a biorepository (Component E of this NOFO) is essential for providing the biospecimens necessary to address gaps in knowledge in the associations of ASD with both maternal immune factors and genetic factors.

Purpose

The purpose of this NOFO is to gain knowledge about ASD, including risk factors for and the expression of ASD, from childhood through early adulthood, and to obtain information that can be used to improve the health and functioning of individuals with ASD as they mature. This will be completed through 1) analysis of existing data and biospecimens from preschool-aged children and their families who participated the CDC funded study known as the Study to Explore Early Development (SEED), a multi-phase, multi-site, case-control study of children identified at age 2-5 years with ASD, other developmental disabilities (DD), and from the general population (POP); and 2) through longitudinal follow-up and research of previous SEED participants to obtain information through early adulthood on their health and functioning, service use and needs, and the impact of ASD on their families.

Healthy People 2030 and other National Strategic Priorities

This NOFO supports the Healthy People 2030 topic areas of Adolescent Health, Disability & Health, and Mental Health & Mental Disorders. This includes the following objectives

- Adolescent Health (AH)
 - AH-9 Reduce the proportion of adolescents and young adults who are neither enrolled in school nor working
- Disability & Health (DH)
 - DH-3 Reduce the proportion of persons with intellectual and developmental disabilities enrolled in publicly funded, long-term services and supports (LTSS) who live in congregate care residences with 7 or more people
 - DH-5 Increase the proportion of students with disabilities who spend at least 80 percent of their time in regular education programs
- Mental Health & Mental Disorders (MHMD)
 - MHMD-2 Reduce suicide attempts by adolescents

- MHMD-3 Increase the proportion of children with mental health problems who receive treatment
- MHMD-6 Increase the proportion of adolescents with major depressive episodes (MDEs) who receive treatment
- MHMD-8 Increase the proportion of primary care office visits where adolescents and adults are screened for depression

Public Health Impact

Information about biologic and environmental risk factors for ASD and the characteristics and needs of persons with ASD and their families will inform strategies to prevent the often debilitating outcomes associated with ASD, as well as strategies to improve the health and functioning of individuals with ASD as they age. Data collected through this NOFO may inform strategies to avoid or eliminate modifiable risk factors for ASD; improve our understanding of which co-occurring conditions are most prevalent; increase our understanding of the needs of individuals with ASD, and how these needs may change with age and can be best met at different points in development; and inform research and public health policies. Specifically, research through this NOFO will provide data to inform public policies on eligibility for needed services and public health outreach efforts that could provide opportunities for education, employment and social connection to improve the health, functioning, and quality of life among persons with ASD and their families.

Relevant Work

As indicated in the Background and Purpose section of this NOFO, SEED 3 is ongoing in six sites through mid-2021. Five study sites in Colorado, Maryland, North Carolina, Wisconsin, and Missouri are currently funded through CDC (RFA-DD16-001). The sixth SEED 3 study site in Georgia is operated by CDC. Each funded site in the SEED 3 Network conducts ASD research and is required to enroll a specific number of participants in three study groups (ASD, DD, and POP) and collect detailed data on prenatal and early childhood environmental and non-environmental exposures, family and child health and demographics, service utilization, developmental data through in-depth clinic assessments, and biological samples. Two previous SEED study sites in California and Pennsylvania participated in SEED 1 (CDC-RFA-DD06-03) and SEED 2 (DD11-002). Funding through this current NOFO allows for analysis of data from the completed SEED (SEED 1-2) study phases, and in combination with SEED 3 data currently being collected, provides ongoing analytic opportunities to address the objectives of SEED. In addition, the data collected on children and families who participated in SEED 1-3 provide a baseline for follow-up surveys and research studies (see **Appendix A**).

During SEED 1-3, biospecimens from participants were collected, processed and maintained for long-term storage. During SEED 1-2, both blood and buccal (SEED 1) or saliva (SEED 2) samples were collected from children and their biological mothers and fathers. During the first half of SEED 3, saliva and blood were collected from children and their biological mothers, and saliva from fathers when available in the ASD and population control (POP) groups. However, no samples were collected from participants in the group of children with other developmental disabilities (DD), and blood collection was discontinued midway through SEED 3 for all participants.

For samples collected, a number of specimen types were frozen, including PAXgene samples, buffy coat, plasma, serum, cell pellets, peripheral blood mononuclear cells (PBMC), red blood cells (RBC), white blood cells (WBC), DNA (from buccal, saliva, buffy coat, and/or WBC), RNA derived from PAXgene tubes, and dried blood spots (DBS). In total, an estimated 200,000 aliquots are in long-term storage from biospecimens previously collected from SEED 1-3 participants. These biospecimens are an essential resource for addressing gaps in knowledge of the contribution of maternal immune factors (i.e., autoantibodies) and genetics to ASD.

In addition to the SEED 1-3 studies of preschool children, during SEED 3, a pilot study, known as SEED Teen, was implemented to follow SEED 1 participants at age 11 to 14 years and is ongoing through mid-2021. Through this pilot study, data are being collected on a subset of the original SEED 1 sites (Georgia, Maryland, North Carolina, and Pennsylvania), thus providing the opportunity to assess ASD-associated outcomes in pre- and early adolescence.

Scientific aims of the SEED Teen pilot study are to

1. Understand the long-term health, functioning, educational achievement, and support needed among children identified at young ages as having ASD in comparison to children identified as having other developmental disabilities and children from the general population;
2. Understand the developmental trajectory of children identified at young ages as having ASD;
3. Establish a mechanism to maintain contact for future follow-up studies of the cohort (i.e., SEED 1 birth cohort) as they began to transition to adulthood.

An important preliminary outcome of SEED Teen is the demonstration that follow-up studies of SEED participants are feasible. While the SEED Teen study is ongoing, as of the second quarter of FY2020, contact has been established with approximately 90% of eligible participants invited. Of those contacted, over 75% have enrolled, and of those enrolled who have had sufficient time to complete the study, 84% (57% of the original participants) have finished the complete data collection protocol.

Additional follow-up data on SEED 1 participants as they approach late adolescence and early adulthood and participants in SEED 2 and 3 birth cohorts get older (see **Appendix A**) provides a unique opportunity to better understand the specific medical, mental health, and behavioral conditions and service needs that may emerge at different developmental periods (i.e., childhood, adolescence, and young adulthood).

2. Approach

The Study to Explore Early Development (SEED) Follow-up Study will collect information from follow-up surveys and in-person assessments on the health and functioning of individuals during childhood, adolescence, and young adulthood. Eligible participants will include those who were previously identified at ages 2-5 years with ASD, other developmental disabilities (DD), and in the general population (POP) through their participation in the original SEED 1-3 studies, as shown in **Appendix A**. Specific areas of health and functioning to be collected through the surveys and in-person assessments are shown in **Appendix B**. Awardees are expected to implement certain project components, including participation in SEED work groups and committees, data collection, project staffing, laboratory and data analyses, and

reporting. The expected outcome is to produce high-quality data and analyses that can be used to establish an evidence base to inform research and public health strategies to improve the health, functioning, and quality of life for individuals with ASD and their families.

This NOFO includes five separate funding components to meet program goals:

- Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants;
- Component B: In-Person Assessment of Intellectual Abilities of SEED Participants;
- Component C: Maternal Auto-Antibody Testing;
- Component D: Genetic Analyses;
- Component E: Biorepository.

Applicants may apply for multiple components but must submit a separate application for each component. Periods of performance for each component are as follows:

- Component A: 7/1/2021 - 6/30/2026 (Budget Years 1-5);
- Component B: 7/1/2021 - 6/30/2025 (Budget Years 1-4);
- Component C: 7/1/2021 - 6/30/2024 (Budget Years 1-3);
- Component D: 7/1/2021 - 6/30/2026 (Budget Years 1-5);
- Component E: 7/1/2021 - 6/30/2026 (Budget Years 1-5).

To be funded for Components B, C, D, or E, applicants must apply for and be funded for Component A. A separate application is required for each component.

To conduct analyses of existing data for Component A, after award, CDC will provide awardees restricted access to a de-identified pooled data set through a centralized web-based system that meets Federal standards for security and confidentiality.

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants.

5-year Period of Performance (7/1/2021 - 6/30/2026)

Component A awardees are expected to participate in SEED meetings, conference calls and workgroups to provide individual input and advice on research gaps in risk factors for ASD and the characteristics and needs of children with ASD that can be addressed using existing SEED data; conduct and report results of priority analyses of existing SEED data, including publication and data verification; and support the conduct of standardized follow-up surveys, (**Appendix B**) including: i) an initial follow-up survey of parents from SEED 1-3; ii) a second follow-up survey of parents of adult children from SEED 1 (to assess changes in services at anticipated time of exit from school); and iii) a direct survey of adult children from SEED 1 (to obtain self-reported data).

Requirements for Component A:

Note: unless otherwise specified, the requirements are for the entire 5-year period of performance.

1. Provide Individual Site Input into Guidelines for Data Sharing and Publication (Funding Year 1). Awardees are expected to collaborate with other Component A awardees and CDC to

provide individual site input for updating the *Data Sharing and Publication Guidelines for Analysis, Presentation, Publication, and Release of SEED Data* (available upon request -- see Section VII. Agency Contacts, Scientific/ Research Contact(s) Marcella Law to obtain a copy), taking into account CDC publication requirements and Federal data sharing guidelines.

2. *Participate in Annual Meetings* (online or in person as planned each year) to work collaboratively with funded awardees and CDC to

- a. Re-assess and prioritize analysis proposals to address gaps in literature that can be addressed by SEED data;
- b. Discuss and resolve issues related to study implementation;
- c. Present ongoing analyses.

3. *Participate in Monthly Conference Calls of the SEED Data Sharing Committee*. At least one representative for each awardee is expected to serve on the SEED Data Sharing Committee and provide individual site review of all analysis proposals (known as Letters of Intent, or LOIs) for the use of SEED data.

4. *Submit Proposals for Analysis of SEED Data*. Awardees are expected to submit proposals and obtain approval from the SEED Data Sharing Committee for at least one LOI in Year 1 and two LOIs each year in Year 2-5.

- a. SEED data refers to data from SEED 1-3, SEED Teen, or SEED data collected under the current NOFO (Funding Year 5).
- b. LOIs are expected to provide an overview of what is known about the topic (brief literature review), what is added by the proposed analysis, variables to be included, statistical methods, and evidence of sufficient sample size for analysis objectives.
- c. At least one LOI each year is expected to address a high priority topic as established under Requirement 2, above.

5. *Complete High-Priority Analyses of SEED Data*. Each awardee is expected to complete at least one analysis each year in Year 1-2 and two analyses each year in Year 3-5 using SEED data (SEED 1-3, SEED Teen or SEED data collected under the current NOFO [Funding Year 5]). At least one analysis per year is expected to address a high priority research topic established under Requirement 2, above.

6. *Prepare Manuscripts Based on SEED Data*. This includes approval through CDC clearance and/or submission to a journal for peer-review, and provision of an informational copy to other Component A and previous SEED awardees (to comply with original data sharing agreements). At least one manuscript is expected each year in Year 1-2 and at least 2 manuscripts in Year 3-5.

7. *Provide Code for All Manuscripts Based on SEED Data*. For all manuscripts accepted for publication, the lead author or analyst is expected to submit documentation of the analysis and final code to CDC, according to the specifications, for data reproducibility and establishment of a shared library of re-coded variables.

8. *Provide Individual Site Input into the Development of Standardized Assessment Tools and Study Protocols* (Funding Year 1). Work collaboratively with other Component A awardees and CDC to fully develop content for the SEED Follow-up Surveys (as outlined in **Appendix B**),

and study implementation procedures including:

- a. Participate in an in-person or virtual kickoff meeting;
- b. Participate in regularly scheduled conference calls to review outcomes aligning with research priorities, refine measures to be collected in surveys, and develop protocols for obtaining consent from adult children for surveys.

9. *Obtain IRB Approval* (Funding Year 1). Each awardee is expected to collaborate with CDC to obtain IRB approval for study implementation under the new Common Rule requiring a single IRB approval for cooperative (i.e., multi-institutional) agreements in the United States. Applicants must document ability to include

- a. Consent to share identifiable, individual-level contact information (i.e., personally identifiable information (PII) -- including addresses and telephone numbers) with a central interviewing contractor;
- b. Approval on protocols for obtaining informed consent from adult children from SEED.

10. *Collaborate with a Central Interviewing Contractor and CDC to Develop Electronic Data Systems for Participant Tracking and Survey Data Collection* (Funding Year 1).

- a. Work with a central interviewing contractor to develop, test, and use a secure method for sharing participant contact information and study progress data (e.g., a File Transfer Protocol (FTP) site or encrypted email -- the contractor will be responsible for implementing the secure mechanism);
- b. Participate in pilot testing for computer-assisted telephone interviews (CATI) and any other data capture systems developed by the central interviewing contractor;
- c. Provide feedback to the central interviewing contractor on all data systems, manuals and guidance as requested.

11. *Trace Contact Information for SEED 1-3 Participants and Mail Survey Invitations* (Funding Years 2-4). Component A funding awardees are expected to identify updated contact information for all eligible SEED 1-3 participants from at least one cohort of the original SEED 1-3 study sites, mail initial invitation packets, and collaborate with a central interviewing contractor to reach no less than 90% of eligible participants at the site(s). To do this, awardees are expected to

- a. Generate a list of all eligible SEED 1-3 participants based on the following criteria
 - i. **Child participated in SEED 1, 2, or 3 and received a final classification of ASD, DD or POP was enrolled in SEED 1-3 and completed the clinic visit**
 - ii. Primary caregiver or mother consented to be contacted in the future for possible follow-up studies;
- b. Mail introductory packets to all eligible participants as an initial invitation to participate in the follow-up surveys;
- c. Inform the central interviewing contractor of returned invitation packets and provide any available information to support tracing additional contact information for potential participants with the goal of establishing contact with no less than 90% of all eligible

participants.

12. Collaborate with a Central Interviewing Contractor to Enroll and Maintain Contact with SEED Follow-up Study Participants (Funding Year 2-5). Awardees are expected to collaborate with a central interviewing contractor to enroll no less than 75% of eligible SEED participants of at least one cohort from the original SEED 1-3 study who are successfully contacted for the first follow-up survey. Additionally, they are expected to assist the contractor in maintaining contact with eligible SEED 1 participants to achieve no less than a 40% completion rate for the second follow-up surveys (parent and adult child).

- a. Depending on awardee IRB regulations and approvals, within 7-14 days of mailing the invitation packet, awardees are expected to complete either activity i or ii listed below:
 - i. Conduct telephone calls to contact the participant and obtain permission to share PII with the central interviewing contractor (i.e., pre-consent); on a weekly basis, awardees are expected to send to the central interviewing contractor
 - a. a list of interested and eligible participants, including their name, the date of pre-consent, and their telephone numbers;
 - b. a list of participants who were contacted and refused participation;
 - c. a list of eligible participants who could not be contacted and need additional tracing to identify a working phone number and address.
 - ii. Provide information for the central interviewing contractor to attempt to contact eligible participants by telephone and enroll participants without pre-consent; on a weekly basis, awardees are expected to send to the central interviewing contractor
 - a. a list of eligible participants to whom invitation packets were mailed, including their names, the date the packet was mailed, and their telephone numbers;
 - b. a list of eligible participants for whom mail was returned as undeliverable.
- b. Meet by phone or web with the central interviewing contractor on a bi-weekly basis to discuss study progress and troubleshoot any problems with study implementation.
- c. Serve as the point of contact for interested and enrolled participants throughout implementation of the initial and the second follow-up surveys; work collaboratively with the central interviewing contractor to maximize participant retention for the second follow-up surveys, including the second survey of parents and adult children of SEED 1. This includes implementation of strategies to retain participants of diverse racial-ethnic and demographic backgrounds.

13. Maintain Adequate Staffing. Each awardee is expected to ensure appropriate and adequate staffing to support statistical analysis and reporting, survey conduct, and project operations and leadership, including expertise in epidemiology, maternal and child health, public health, developmental disabilities, and biostatistics, as well as at least one specialty area in child psychiatry, clinical psychology, developmental psychology, pediatric medicine, or genetics.

14. Contribute Site-specific Data to a Pooled Dataset that is maintained and overseen by CDC and accessed through a CDC-approved mechanism. Component A awardees are expected to contribute site-specific data to a pooled SEED data set. This pooled data set will be maintained

and overseen by CDC according to a standard SEED Data Management Plan that meets Federal data sharing requirements and will be accessed by awardees and previous SEED sites through a CDC-approved mechanism that meets Federal standards for security and confidentiality.

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants.

4-year Period of Performance (7/1/2021 - 6/30/2025)

Component B awardees are expected to conduct an in-person follow-up assessment (**Appendix B**) of intellectual abilities on a subset of children and adolescents (age ≥ 8 years) **who meet the following eligibility criteria: (1) received a final class of ASD or DD in SEED 1, 2, or 3; (2) completed the clinic visit, including the Mullen Scales of Early Learning, during SEED 1, 2 or 3; and (3) completed the first follow-up survey** in Component A of this NOFO. To be funded for Component B, applicants must apply and be funded for Component A.

Requirements for Component B:

Note: unless otherwise specified, all requirements are for the entire 4-year period of performance. If psychometric assessments cannot be conducted in person due to safety reasons, alternatives can be proposed.

1. Provide Individual Site Input into the Development of Standardized Assessment Tools and Study Protocols (Funding Year 1). Work collaboratively with other Component B awardees and CDC to fully develop content for the in-person assessments (as outlined in Appendix B), and study implementation procedures.

- a. Participate in an in-person or virtual kickoff meeting;
- b. Participate in regularly scheduled conference calls to review outcomes aligning with research priorities, refine measures to be collected, and develop protocols.

2. Hire, Train, and Maintain Component B Personnel (Funding Year 2-4). Component B awardees are expected to hire and train an investigator with expertise to train psychometrists, determine their field readiness, evaluate administration fidelity and scoring reliability, and answer questions from participants and families.

3. Enroll and Maintain Contact with Participants (Funding Year 2-4). Component B awardees are expected to implement strategies to encourage enrollment and maintain contact with SEED Follow-up Study participants, including strategies to retain participants of diverse racial-ethnic and demographic backgrounds.

4. Conduct In-Person Assessments (Funding Year 2-4). Component B awardees are expected to administer standardized psychometric assessments on at least 100 participants. These participants must have been identified as having ASD or DD in SEED 1-3, and at least 50% of completions must be from the ASD group. The central interviewing contractor will provide a list of interested participants. Component B awardees are expected to employ staff for scheduling, obtaining informed consent, and administering a standardized psychometric assessment of approximately 90-minutes in length.

5. Generate and Provide Feedback Letters (Funding Year 2-4). Provide parents feedback on results of the psychometric assessment by sending a standardized feedback letter to Component B participants within one month of the psychometric assessment.

6. Maintain Confidentiality of Study Documents and Contribute to a Pooled Dataset that is

maintained and overseen by CDC and accessed through a CDC-approved mechanism. Awardees must store, enter, and transmit relevant data in a standardized and secure manner with common elements mutually agreed upon by CDC and Component B awardees. This will become part of a pooled data set and will be maintained and overseen by CDC according to a standard SEED Data Management Plan that meets Federal data sharing requirements and will be accessed by awardees and previous SEED sites through a CDC-approved mechanism to meet Federal standards for security and confidentiality.

Component C: Maternal Auto-Antibody Testing

3-year Period of Performance (7/1/2021 - 6/30/2024)

The Component C awardee is expected to conduct assays of maternal autoantibodies (MABs) known to be reactive to proteins in the fetal brain using stored SEED 1-2 samples, and conduct analyses of the association between MABs and ASD to better understand their contribution to ASD risk and ASD phenotypes. To be funded for Component C, applicants must apply and be funded for Component A.

Requirements for Component C:

Note: unless otherwise specified, the requirements are for the entire 3-year period of performance.

1. Conduct MAB Assays. The Component C awardee is expected to conduct and complete assays measuring MABs known to be reactive to eight target proteins in the fetal brain with an established role in neurodevelopment [65]. Nearly 1,300 serum and/or plasma samples are available from maternal SEED 1-2 participants who have children who were identified with ASD, and nearly 1,400 maternal participants who have children from the general population. Completion targets will include MAB assays on samples from 1,200 SEED participants in the first year of the period of performance, 1,200 in the second year, and 300 in the third year.

2. Implement an Analytic Agenda. The awardee is expected to develop and implement an analytic plan for exploring the association between MABs reactive to fetal proteins and ASD in collaboration with CDC and other awardees.

3. Submit Proposals for Data Analyses. At minimum, over the entire period of performance, in collaboration with other awardees and CDC, the Component C awardee is expected to develop and obtain approval from the SEED Data Sharing Committee for three Letters of Intent related to the MAB data (LOIs; for more information about Letters of Intent, see Component A, requirement 4 [*Submit Proposals for Analysis of SEED Data*]). The requirement for submitting and obtaining approval for LOIs related to MABs will be in addition to the requirement for LOIs to be approved under Component A.

4. Analyze Data and Present Findings (Funding Year 3). The awardee will be expected to conduct an analysis of the main findings of the MAB assays of SEED 1-2 participants in collaboration with CDC and other awardees. The completion target for this objective will be a presentation of preliminary findings of analyses to investigators in the SEED Network, or at a relevant professional conference.

5. Maintain Confidentiality and Contribute to a Pooled Dataset. The Component C awardee must store, enter, and transmit results of specimen testing and relevant data in a standardized and secure manner with common data elements mutually agreed upon with CDC. This will

become part of a pooled data set and will be maintained and overseen by CDC according to a standard SEED Data Management Plan that meets Federal data sharing requirements. This data will be accessed by awardees and previous SEED sites through a CDC-approved mechanism that meets Federal standards for security and confidentiality.

Component D: Genetic Analyses

5-year Period of Performance (7/1/2021 - 6/30/2026)

The Component D awardee is expected to identify analytic priorities for SEED genetic data; to develop and implement methods for combining existing SEED 1 genetic data with potentially generated SEED 2-3 genetic data for use by SEED investigators and contribution to data repositories; and to support SEED investigators conducting analyses to increase understanding of the genetic risk factors of ASD and their interactions with environmental risk factors. To be funded for Component D, applicants must apply and be funded for Component A.

Requirements for Component D:

Note: unless otherwise specified, the requirements are for the entire 5-year period of performance.

- 1. Establish Priorities for Use of SEED Biospecimens and an Analytic Agenda* (Funding Year 1). The Component D awardee is expected to participate in an in-person or virtual expert workgroup meeting to provide individual input and expert advice on an analytic agenda for prioritizing SEED genetic and epigenetic analyses. This workgroup will consist of the Component D PI and co-investigators, Component A awardees with expertise in genetics, CDC personnel, and consultants selected by the CDC from external agencies such as the National Institutes of Health for their expertise in genetic contributions to ASD. To prepare for these meetings the awardee is expected to conduct scans of the literature to identify gaps in knowledge and statistical power analyses to inform which questions can be addressed with SEED 1 data alone, which will require the combined SEED 1-3 data set, and which will require meta-analyses of SEED data with ASD-related genetic data from non-SEED studies.
- 2. Develop Collaborations with Genetics Researchers Involved in ASD Research.* The Component D awardee is expected to collaborate with ASD researchers with genetic expertise and CDC to explore the potential for SEED data to be included in data repositories and/or meta-analyses for the mutual benefit of obtaining genetic data for SEED and for contributing data for addressing hypotheses beyond the scope of objectives for SEED (i.e., the contribution of rare genetic variants to ASD).
- 3. Provide Oversight for Genotype Data Processing, Including Development of New Analytic Pipelines.* The Component D awardee is expected to support genotype data pre-processing and pipeline development for data newly obtained from SEED 2-3 biospecimens. Activities will include, but are not limited to, generating raw genotype reads, implementing quality control filters, controlling for batch effects, imputing variants not genotyped directly, and harmonizing datasets genotyped across years on platforms with varying SNP (single nucleotide polymorphism) coverage, including data previously obtained from SEED 1 biospecimens.
- 4. Create Derived Genetic Variables.* The Component D awardee is expected to provide analytic support for creating a set of derived variables for copy number variant (CNV), SNP, and polygenetic risk score (PRS) level analyses.

5. *Provide Access to High-Capacity Computer Servers.* In addition to conducting the analytic work for creating derived genetic variables, the awardee is expected to provide secure access to high-capacity computing servers for approved SEED investigators with expertise to contribute to the development of these variables.

6. *Contribute Final Derived Genetic Variables to a Pooled Dataset.* The Component D awardee is expected to contribute final derived genetic variables to a pooled data set maintained and overseen by CDC according to a standard SEED Data Management Plan that meets Federal data sharing requirements that will be accessed by Component A awardees and previous SEED sites through a CDC-approved mechanism that meets Federal standards for security and confidentiality.

7. *Provide Analytic Support for Genetic Analyses.* The Component D awardee is expected to provide analytic support for approved SEED investigators conducting genetic analyses. In this role, it is expected that the Component D awardee will maintain expertise on the latest analytic methods that can be shared with approved SEED investigators. It is expected that the awardee serve as the primary analyst or as a supporting co-author on two LOI submissions each year involving genetic or epigenetic data. The requirement supporting two LOIs involving genetic or epigenetic data will be in addition to the requirement under Component A.

Component E: Biorepository

5-year Period of Performance (7/1/2021 - 6/30/2026)

The Component E awardee is expected to support the continued maintenance, storage, and accessibility of the estimated 200,000 aliquots obtained during SEED 1-3 in a single biorepository, while ensuring the safety and security of all samples and the confidentiality of participants. To be funded for Component E, applicants must apply and be funded for Component A.

Requirements for Component E:

All requirements are for the entire 5-year period of performance.

1. *Ensure Long-term Preservation of the SEED Biorepository.* The awardee is expected to maintain and ensure the long-term preservation of biospecimens collected during SEED 1-3.

2. *Provide Sample Accounting, Retrieval and Long-Term Planning.* The awardee is expected to implement a tracking system that maintains confidentiality for participants and provides timely and accurate accounting of samples. In addition, the awardee is expected to retrieve samples for shipment to other laboratories for all uses approved by CDC and previous SEED awardees involved in their collection, per current agreements for the use of SEED biospecimens. The awardee is expected to provide an accounting of the samples within 2 months of any such request for their retrieval. In addition, the awardee is expected to provide a report with a full accounting of all samples in the biorepository twice each year and to develop contingency plans for maintaining the SEED Biorepository should they become unable to do so.

Objectives/Outcomes

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants

Objectives:

1. To collaborate with other awardees and CDC to conduct comprehensive, high-quality, analyses of SEED data based on a written priority list designed to address key research gaps and improve our understanding of the risk factors for ASD and the characteristics and needs of preschool age children with ASD.
2. To ensure data are of high scientific quality and comparable to other sites by following a common methodology established with CDC and other awardees.
3. To implement methods to ensure high participation rates among parents of previous SEED participants and adult SEED participants and maximize the number of completed follow-up surveys.
4. To collect and analyze standardized, high-quality information via parental and participant telephone interviews to inform further research and improve key outcomes for children with ASD and their families relative to children with other developmental disabilities (DD) and children in the general population (POP), including the
 - Trajectory of preschool children as they age, including their health, educational attainment, and level of functioning;
 - Healthcare utilization and needs of children, adolescents, and young adults;
 - Educational and social needs and service utilization of children, adolescents, and young adults;
 - Factors associated with key outcomes in children, adolescents, and young adults -- including, but not limited to, co-occurring conditions, health care utilization, educational attainment, and social supports;
 - Impacts on families and service needs associated with having a child with ASD at various life stages, from early childhood to early adult years.
5. To interpret and disseminate analytic results to expand the evidence base that can inform research and public health action.

Expected Outcomes:

1. Analyze and disseminate SEED data on a variety of topics to improve understanding of the risk factors for ASD, the characteristics and needs of children aged 2-5 years with ASD, and the characteristics, needs and family impacts of children identified with ASD at an early age through early adulthood.
2. Produce timely, high-quality data representative of previous SEED participants to inform research and public health strategies to improve the health, functioning, and quality of life for individuals with ASD and their families.

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

Objectives:

1. To implement high-quality, standardized, in-person assessments of intellectual abilities for participants from at least one of the original SEED 1-3 sites.
2. To ensure the data collected are of high scientific quality and comparable to that for other Component B awardees.

3. To ensure data are available for analyses by all SEED 1-3 study investigators.

Expected Outcomes:

1. Produce timely, high-quality, standardized data on intellectual abilities for a subsample of children in SEED.
2. Make SEED data on intellectual abilities available to all SEED 1-3 study investigators for research to contribute to a better understanding, among children with ASD and other developmental disabilities, of the following:
 - Potential changes in intellectual abilities from preschool to early childhood and adolescence;
 - Early childhood predictors of future intellectual functioning;
 - Extent to which adolescent outcomes may be mediated by intellectual functioning skills;
 - Discrepancy between intellectual and executive functioning and adaptive behavior collected in Component A, and variables associated with that discrepancy if any;
 - Systematic and random error in parental reports of intellectual abilities.

Component C: Maternal Auto-Antibody Testing

Objectives:

1. To complete high-quality and relevant MAB assays on SEED 1-2 biospecimens.
2. To ensure data from MAB assays can be used with a pooled dataset of other SEED data and are available for use by CDC and all SEED investigators.
3. To conduct comprehensive data analyses of MABs in combination with other SEED data to address relevant research gaps to increase our understanding of ASD.
4. To disseminate analytic results to inform research and public health practice related to ASD.

Expected Outcomes:

1. Produce timely, high-quality data on MABs for selected SEED participants to expand our understanding of maternal immune factors and ASD.
2. Make data on MABs available for research to increase our understanding of risk factors for ASD.
3. Analyze and disseminate SEED data on MABs to expand the understanding as to whether:
 - MABs reactive to fetal brain proteins are associated with increased ASD risk;
 - An association of certain MABs both with increased ASD risk and maternal conditions previously found to be associated with ASD (i.e., maternal auto-immune disorders, infections, and maternal metabolic conditions during pregnancy, including maternal obesity, gestational diabetes and hypertensive disorders) offers a potential mechanism by which these maternal conditions may increase ASD risk; and
 - Certain MABs are associated with and provide a potential mechanism to account for particular ASD sub-phenotypes.

Component D: Genetic Analyses

Objectives:

1. To identify analytic priorities for generating and analyzing SEED genetic data in order to increase the understanding of genetic risk factors for ASD.
2. To develop and implement methods for combining existing SEED 1 genetic data and SEED 2 and 3 genetic data that are newly generated based on priorities set for use by SEED investigators and contribution to data repositories.
3. To expand and enhance analyses and dissemination of SEED data on the genetic risk factors for ASD and their interaction with environmental factors to inform knowledge gaps and increase the understanding of health and functional outcomes of children with ASD.

Expected Outcomes:

1. Implement analytic priorities and action plans for establishing collaborations with ASD researchers with genetic expertise, including prioritization of use of SEED 2-3 biospecimens for generating genetic and epigenetic data.
2. Establish collaborative relationships with other ASD researchers with genetic expertise and resources in order to facilitate the contribution of SEED 1-3 samples to genetic analysis for the mutual benefit of obtaining genetic data for SEED and contributing data for addressing hypotheses beyond the scope of objectives for SEED (i.e., the contribution of rare genetic variants to ASD).
3. Analyze and disseminate SEED genetic data to increase the understanding of cumulative effects of common genetic variant and gene by environment interactions in association with ASD, including, for example, obstetric factors and environmental exposures surrounding pregnancy.

Component E: Biorepository

Objectives:

1. To ensure long-term preservation of the SEED biorepository and biospecimens.
2. To maintain a secure tracking system that ensures participant confidentiality.
3. To ensure timely, safe, secure, and efficient retrieval of samples as needed for genetic and other analyses.

Expected Outcomes:

1. Ensure specimens are preserved, available, and can be used in a timely and efficient manner for analyses of biological risk factors in association with ASD.
2. Provide previously collected biospecimens to address gaps in knowledge in the associations of ASD with both maternal immune factors and genetic factors.
3. Document availability of specimens within the SEED biorepository.

Target Population

In general, this NOFO is expected to address children, adolescents, and young adults with ASD,

other developmental disabilities, and in the general population. Component B participants and their families will directly benefit by receiving a psychometric evaluation that may help them and their providers understand their level of functioning. In addition, children, adolescents, and young adults with ASD and their families are expected to indirectly benefit from the research and data provided through this NOFO. The data from this NOFO are expected to enhance the understanding of ASD, and inform public policies on eligibility criteria for services and outreach strategies that could provide opportunities for education, employment, and social connection to improve the health, functioning, and quality of life of individuals with ASD and their families.

Components A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants, D: Genetic Analysis, and E:

Biorepository address the population of individuals who were born between 2003-2006, 2008-2012, and 2014-2017 and were identified at ages 2-5 years with ASD, other developmental disabilities, or were part of the general population within the defined geographic study area and participated in SEED 1-3 (See **Appendix A**).

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants addresses the population of individuals who will be aged 8-22 years between 7/1/2022 and 6/30/2025, were identified at ages 2-5 years with ASD or other developmental disabilities within the defined geographic study areas, and participated in SEED 1-3.

Component C: Maternal Auto-Antibody Testing addresses the population of individuals who were born between 2003-2006 and 2008-2012, were identified at ages 2-5 years with ASD or in the general population within the defined geographic study areas, and participated in SEED 1 or SEED 2.

Collaboration/Partnerships

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants

Awardees are expected to engage in collaborative processes and workgroups similar to those established for the implementation of SEED 1-3 studies. Each awardee is expected to have a minimum of one representative for each SEED workgroup or committee. In general, these workgroups and committees meet once a month via conference call or web, but the schedule may change depending on need. In addition, these groups may convene in-person at the annual collaborator meeting. Through these workgroups and committees, Component A awardees are expected to collaborate with each other and CDC; these workgroups will include but are not limited to

1. Principal Investigator Workgroup, to provide individual site input into the design of the SEED follow-up study protocols and instruments;
2. Data Sharing Committee, to review analysis priorities annually along with individual analysis proposals and manuscripts; additionally, in Funding Year 1, awardees are expected to collaborate with each other and CDC to provide individual site input for updating the SEED Data Analysis and Publications Guidelines, taking into account CDC publication requirements and Federal data sharing guidelines;
3. Biologic Monitoring Committee, to provide individual site input on priorities and use of

SEED 1-3 biospecimens;

4. Complex Derived Variable Committee, to provide individual site input on the development of complex re-coded variables with SEED data.

Awardees are expected to work with a central interviewing contractor and CDC to test and utilize electronic data capture systems and to trace, track, and invite participants for follow-up surveys. Awardees also are expected to work with a central interviewing contractor, other Component A awardees, and CDC to develop and implement standardized processes, methods, and data collection procedures.

Component A awardees also are expected to collaborate in contributing their site-specific individual participant data to a shared data pool for use by all SEED investigators and CDC. For this purpose, they are expected to adhere to

1. Site-specific roles and responsibilities for maintaining the confidentiality and security of the personally identifiable information collected as part of SEED;
2. CDC-approved mechanism for accessing pooled, de-identified data through a CDC-approved remote access system meeting Federal standards for maintaining security and confidentiality of participant data.
3. A standard SEED Data Management Plan that meets Federal data sharing requirements.

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

Component B awardees are expected to identify a Supervising Site Clinician to participate in two workgroups with CDC to

1. Discuss and finalize data collection instruments for the in-person visit;
2. Meet once per quarter after clinic visits have begun to discuss clinical issues, questions from the field, and other relevant topics.

Component B awardees are also expected to collaborate in contributing their site-specific individual participant data to a shared data pool for use by all SEED investigators and CDC.

Component C: Maternal Auto-Antibody Testing

The Component C awardee is expected to collaborate with investigators across the SEED Network and CDC in the development of hypotheses and analyses and reports related to the association between MABs and ASD, and MABs and maternal and child characteristics associated with ASD.

Component D: Genetic Analyses

The Component D awardee is expected to collaborate with investigators across the SEED Network and CDC on the development of analysis proposals and conduct of analyses involving genetic data. This will include collaborating with SEED investigators and providing secure access to high-capacity computing servers for those with expertise to contribute to the development of derived variables (CNV, SNP and polygenetic risk scores) related to genetics. Additionally, the Component D awardee is expected to collaborate with ASD researchers with expertise in genetics and CDC to explore the contribution of SEED genetic data to biorepositories for the mutual advancement of SEED objectives and the objectives of other

research projects related to ASD.

Component E: Biorepository

The Component E awardee is expected to support the retrieval and shipping of samples to other laboratories for analysis of SEED biospecimens on an as needed basis.

Evaluation/Performance Measurement

All awardees are expected to create an evaluation plan by 8-months post-award that monitors progress toward completion of the major requirements of each component.

This evaluation plan assesses adherence to obtaining and maintaining appropriate staffing; assesses timeliness, number, and quality of data analyses and manuscripts; monitors achievement of planned sample size goals for access of initial contact information for eligible participants; assesses fidelity to proposed response rates for tracing, contacting, and retaining eligible participants of diverse racial-ethnic groups; assesses adherence to data quality, data confidentiality and security, and data management protocols; analyzes data and demonstrates use of the evaluation parameters in informing system changes and research. Evaluation plans will be refined with collaboration from CDC post-award.

In their overall evaluation plan, awardees of Components B, C, D, and E of this NOFO are expected to include additional parameters to measure their performance as indicated below:

Component B - assess the success of methods for maximizing participation in, and completion of, the assessment of intellectual abilities across diverse racial-ethnic groups; and assess quality of the assessments.

Component C - assess fidelity for assuring high-quality assays, laboratory methods, and quality control.

Component D - assess the success of collaborations to conduct further genetic testing of SEED biospecimens; assess the fidelity of the plan for processing, quality control, and pipeline development for newly generated genetic data from SEED biospecimens; and assess the effectiveness of the plan for providing analytic support for genetic data processing and variable development.

Component E - monitor the maintenance of the biospecimens, as well as the timeliness and accuracy of the procedures for biospecimen tracking, accounting, and retrieval.

Translation Plan

Components A, B, C and D

Awardees are expected to present the findings from research analyses at both scientific and community partner meetings and publish in peer-reviewed journals. Awardees are expected to develop a plan for completion of priority analyses and their dissemination in collaboration with other SEED investigators and CDC as part of their participation in data sharing and the SEED Annual Meeting. The plan should describe

- The priority topics for SEED data analyses;
- How findings will be disseminated through various channels, including at annual meetings, with health policy makers, and health providers;

- How data will inform public health actions to improve the health, functioning, and quality of life of individuals with ASD and their families.

Component E - N/A

OMB/PRA is expected to apply.

References

1. Maenner, M, et al., Prevalence of Autism spectrum disorder among children aged 8 years, Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2016. MMWR Surveill Summ, 2020. **69**: 1-12.
2. Lavelle, TA, et al., Economic burden of childhood autism spectrum disorders. Pediatrics, 2014. **133**: e520-9.
3. Lyall, K, et al., The changing epidemiology of autism spectrum disorders. Annu Rev Public Health, 2017. **38**: 81-102.
4. Shattuck, P. *Growing numbers of youth on the autism spectrum*. Life Course Outcomes Blog [June 2019]; Available from: <https://drexel.edu/autismoutcomes/blog/overview/2019/June/Growing-numbers-of-young-adults-on-the-autism-spectrum/>.
5. Piven, J, P Rabins, and Autism in Older Adults Working Group, Autism spectrum disorders in older adults: Toward defining a research agenda. J Am Geriatr Soc, 2011. **59**: 2151-2155.
6. <https://iacc.hhs.gov/publications/strategic-plan/2017/>.
7. Wiggins, LD, et al., Using standardized diagnostic instruments to classify children with autism in the Study to Explore Early Development. J Autism Dev Disord, 2015. **45**: 1271-1280.
8. Schieve, LA, et al., Maternal and paternal infertility disorders and treatments and autism spectrum disorder: findings from the Study to Explore Early Development. J Autism Dev Disord, 2017. **47**: 3994-4005.
9. Schieve, LA, et al., Associations between the 2nd to 4th digit ratio and autism spectrum disorder in population-based samples of boys and girls: findings from the Study to Explore Early Development. J Autism Dev Disord, 2018. **48**: 2379-2395.
10. Croen, LA, et al., Family history of immune conditions and autism spectrum and developmental disorders: Findings from the Study to Explore Early Development. Autism Res, 2019. **12**: 123-135.
11. Croen, LA, et al., Infection and fever in pregnancy and autism spectrum disorders: findings from the Study to Explore Early Development. Autism Res, 2019. **12**: 1551-1561.
12. Schieve, LA, et al., Autism spectrum disorder and birth spacing: Findings from the Study to Explore Early Development (SEED). Autism Res, 2018. **11**: 81-94.
13. Singer, AB, et al., Maternal exposure to occupational asthmagens during pregnancy and autism spectrum disorder in the Study to Explore Early Development. J Autism Dev Disord, 2016. **46**: 3458-3468.
14. Cordero, C, et al., Maternal diabetes and hypertensive disorders in association with autism spectrum disorder. Autism Res, 2019. **12**: 967-975.
15. Windham, GC, et al., Maternal pre-pregnancy body mass index and gestational weight gain in relation to autism spectrum disorder and other developmental disorders in offspring. Autism Res, 2019. **12**: 316-327.

16. Cordero, C, et al., Neonatal jaundice in association with autism spectrum disorder and developmental disorder. *J Perinatol*, 2020. **40**: 219-225.
17. McGuinn, L and e al., Early life exposure to air pollution and autism spectrum disorder: findings from a multisite case-control study. *Epidemiology*, **31**: 103-114.
18. Rubenstein, E, et al., Associations between parental broader autism phenotype and child autism spectrum disorder phenotype in the Study to Explore Early Development. *Autism*, 2019. **23**: 436-448.
19. Singer, AB, et al., Prenatal alcohol exposure in relation to autism spectrum disorder: findings from the Study to Explore Early Development (SEED). *Paediatr Perinat Epidemiol*, 2017. **31**: 573-582.
20. Wiggins, LD, et al., A phenotype of childhood autism is associated with preexisting maternal anxiety and depression. *Journal of Abnormal Child Psychology*, 2018. **47**: 731-740.
21. Soke, GN, et al., Association between breastfeeding initiation and duration and autism spectrum disorder in preschool children enrolled in the Study to Explore Early Development. *Autism Res*, 2019. **12**: 816-829.
22. McGuinn, L, et al., Air pollution, neighborhood deprivation, and autism spectrum disorder in the Study to Explore Early Development. *Environ Epidemiol*, 2019. **3**: 10.1097.
23. Rubenstein, E, et al., Brief Report: Maternal opioid prescription from preconception through pregnancy and the odds of autism spectrum disorder and autism features in children. *J Autism Dev Disord*, 2019. **49**: 376-382.
24. Ladd-Acosta, C, et al., Presence of an epigenetic signature of prenatal cigarette smoke exposure in childhood. *Environ Res*, 2016. **144**: 139-148.
25. Andrews, SV, et al., Case-control meta-analysis of blood DNA methylation and autism spectrum disorder. *Mol Autism*, 2018. **9**: 40.
26. Mitra, I, et al., Pleiotropic mechanisms indicated for sex differences in autism. *PLOS Genetics*, 2016. **12**: e1006425.
27. Sabourin, KR, et al., Infections in children with autism spectrum disorder: Study to Explore Early Development (SEED). *Autism Res*, 2019. **12**: 136-146.
28. Shapira, SK, et al., A novel approach to dysmorphology to enhance the phenotypic classification of autism spectrum disorder in the Study to Explore Early Development. *J Autism Dev Disord*, 2019. **49**: 2184-2202.
29. Reinhartsen, DB, et al., Expressive dominant versus receptive dominant language patterns in young children: findings from the Study to Explore Early Development. *J Autism Dev Disord*, 2019. **49**: 2447-2460.
30. Reynolds, AM, et al., Sleep problems in 2- to 5-year-olds with autism spectrum disorder and other developmental delays. *Pediatrics*, 2019. **143**: e20180492.
31. Levy, SE, et al., Relationship of weight outcomes, co-occurring conditions, and severity of Autism Spectrum Disorder in the Study to Explore Early Development. *J Pediatr*, 2019. **205**: 202-209.
32. Kral, TV, et al., Early life influences on child weight outcomes in the Study to Explore Early Development. *Autism*, 2019. **23**: 954-962.
33. Barger, B, et al., Temperament similarities and differences: a comparison of factor structures from the behavioral style questionnaire in children with and without autism spectrum disorder. *J Autism Dev Disord*, 2019. **49**: 1749-1762.

34. Wiggins, LD, et al., Brief Report: The ADOS calibrated severity score best measures autism diagnostic symptom severity in pre-school children. *J Autism Dev Disord*, 2019. **49**: 2999-3006.
35. Tian, L, et al., Mapping the relationship between dysmorphology and cognitive, behavioral, and developmental outcomes in children with autism spectrum disorder. *Autism Research*, in press. **in press**.
36. DiGuseppi, C, et al., Injuries in children with autism spectrum disorder: Study to Explore Early Development (SEED). *J Autism Dev Disord*, 2018. **48**: 461-472.
37. Soke, GN, et al., Brief Report: Self-Injurious behaviors in preschool children with autism spectrum disorder compared to other developmental delays and disorders. *J Autism Dev Disord*, 2018. **48**: 2558-2566.
38. Soke, GN, et al., Self-injurious behaviors in children with autism spectrum disorder enrolled in the Study to Explore Early Development. *Autism*, 2017. **22**: 625-635.
39. Wiggins, LD, et al., Wandering among preschool children with and without autism spectrum disorder. *J Dev Behav Pediatr*, 2020. **41**: 251-257.
40. Moody, EJ, et al., Screening for autism with the SRS and SCQ: variations across demographic, developmental and behavioral factors in preschool children. *J Autism Dev Disord*, 2017. **47**: 3550-3561.
41. Rubenstein, E, et al., The broader autism phenotype in mothers is associated with increased discordance between maternal-reported and clinician-observed instruments that measure child autism spectrum disorder. *J Autism Dev Disord*, 2017. **47**: 3253-3266.
42. Rubenstein, E, et al., The prevalence of gluten free diet use among preschool children with autism spectrum disorder. *Autism Res*, 2018. **11**: 185-193.
43. DiGuseppi, C, et al., Injury-related treatments and outcomes in preschool children with autism spectrum disorder: Study to Explore Early Development (SEED). *Res Autism Spectr Disord*, 2019. **66**: 101413.
44. Rubenstein, E, et al., Community-based service use in preschool children with autism spectrum disorder and associations with insurance status. *Res Autism Spectr Disord*, 2019. **66**: 101410.
45. Shattuck, P, et al., A national research agenda for the transition of youth with ASD. *Pediatrics*, 2018. **141**: s355-s361.
46. Laxman, DJ, et al., Loss in services precedes high school exit for teens with autism spectrum disorder: A longitudinal study. *Autism Res*, 2019. **12**: 911-921.
47. Dudley, KM, et al., Understanding service usage and needs for adults with ASD: the importance of living situation. *J Autism Dev Disord*, 2019. **49**: 556-568.
48. Shattuck, PT, et al., Postsecondary education and employment among youth with an autism spectrum disorder. *Pediatrics*, 2012. **129**: 1042-1049.
49. Magiati, I, XW Tay, and P Howlin, Cognitive, language, social and behavioural outcomes in adults with autism spectrum disorders: a systematic review of longitudinal follow-up studies in adulthood. *Clin Psychol Rev*, 2014. **34**: 73-86.
50. Eaves, LC and HH Ho, The very early identification of autism: outcome to age 4 1/2 to 5. *J Autism Dev Disord*, 2004. **34**: 367-378.
51. Flanagan, HE, et al., Stability and change in the cognitive and adaptive behaviour scores of preschoolers with autism spectrum disorder. *J Autism Dev Disord*, 2015. **45**: 2691-703.

52. Hedvall, A, et al., Autism and developmental profiles in preschoolers: stability and change over time. *Acta Paediatr*, 2014. **103**: 174-181.
53. Turner, LM, et al., Follow-up of children with autism spectrum disorders from age 2 to age 9. *Autism*, 2006. **10**: 243-265.
54. Chamorro Premuzic, T, et al., Assessing pupils' intelligence through self, parental, and teacher estimates. *Educ Psychol*, 2009. **29**: 83-97.
55. Chandler, S, et al., Emotional and behavioural problems in young children with autism spectrum disorder. *Dev Med Child Neurol*, 2016. **58**: 202-208.
56. Bernheimer, LP, BK Keogh, and D Guthrie, Young children with developmental delays as young adults: predicting developmental and personal social outcomes. *Am J Ment Retard*, 2006. **111**: 263-272.
57. Gillespie-Lynch, K, et al., Early childhood predictors of the social competence of adults with autism. *J Autism Dev Disord*, 2012. **42**: 161-174.
58. Keogh, BK, LP Bernheimer, and D Guthrie, Children with developmental delays twenty years later: where are they? How are they? *Am J Ment Retard*, 2004. **42**: 161-174.
59. Pierce, K, et al., Evaluation of the diagnostic stability of the early autism spectrum disorder phenotype in the general population starting at 12 months. *JAMA Pediatr*, 2019. **173**: 578-587.
60. Alvares, GA, et al., The misnomer of 'high functioning autism': Intelligence is an imprecise predictor of functional abilities at diagnosis. *Autism*, 2020. **24**: 221-232.
61. Duncan, AW and SL Bishop, Understanding the gap between cognitive abilities and daily living skills in adolescents with autism spectrum disorders with average intelligence. *Autism* 2015. **19**: 64-72.
62. Kenworthy, L, et al., Adaptive behavior ratings correlate with symptomatology and IQ among individuals with high-functioning autism spectrum disorders. 2010. **40**: 416-423.
63. Meyer, AT, et al., Brief report: developmental trajectories of adaptive behavior in children and adolescents with ASD. *J Autism Dev Disord*, 2018. **48**: 2870-2878.
64. Gata-Garcia, A and B Diamond, Maternal antibody and ASD: clinical data and animal models. *Front Immunol*, 2019. **10**: 1129.
65. Braunschweig, D, et al., Autism-specific maternal autoantibodies recognize critical proteins in developing brain. *Transl Psychiatry*, 2013. **3**: e277.
66. Jones, KL and J Van de Water, Maternal autoantibody related autism: mechanisms and pathways. *Mol Psychiatry*, 2019. **24**: 252-265.
67. Pantham, P, IL Aye, and TL Powell, Inflammation in maternal obesity and gestational diabetes mellitus. *Placenta*, 2015. **36**: 709-715.
68. Bai, D, et al., Association of genetic and environmental factors with autism in a 5-country cohort. *JAMA Psychiatry*, 2019. **76**: 1035-1043.
69. Kim, YS and BL Leventhal, Genetic epidemiology and insights into interactive genetic and environmental effects in autism spectrum disorders. *Biol Psychiatry*, 2015. **77**: 66-74.
70. Bourgeron, T, From the genetic architecture to synaptic plasticity in autism spectrum disorder. *Nat Rev Neurosci*, 2015. **16**: 551-563.
71. de la Torre-Ubieta, L, et al., Advancing the understanding of autism disease mechanisms through genetics. *Nat Med*, 2016. **22**: 345-361.
72. Buxbaum, JD, et al., The autism sequencing consortium: large-scale, high-throughput sequencing in autism spectrum disorders. *Neuron*, 2012. **76**: 1052-1056.

73. Satterstrom, FK, et al., Large-scale exome sequencing study implicates both developmental and functional changes in the neurobiology of autism. *Cell*, 2020. **180**: 568-584 e23.
74. Gaugler, T, et al., Most genetic risk for autism resides with common variation. *Nat Genet*, 2014. **46**: 881-885.
75. Cross-Disorder Group of the Psychiatric Genomics Consortium, et al., Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nat Genet*, 2013. **45**: 984-994.
76. Zuvich, RL, et al., Pitfalls of merging GWAS data: lessons learned in the eMERGE network and quality control procedures to maintain high data quality. *Genet Epidemiol*, 2011. **35**: 887-898.

Section II. Award Information

Funding Instrument Type:

Cooperative Agreement

A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, scientific or program staff will assist, guide, coordinate, or participate in project activities.

Application Types Allowed:

New - An application that is submitted for funding for the first time. Includes multiple submission attempts within the same round.

Estimated Total Funding:

\$16,370,000

The estimated total funding (direct and indirect costs) for the period of performance, 7/1/2021 - 6/30/2026, is \$16,370,000.

The estimated total funding (direct and indirect costs) for the first budget period, 7/1/2021 - 6/30/2022, is \$3,290,000.

- Component A: \$2,550,000
- Component B: \$40,000
- Component C: \$200,000
- Component D: \$450,000
- Component E: \$50,000

Anticipated Number of Awards:

11

The estimated total funding (direct and indirect costs) for the first budget period, 7/1/2021 - 6/30/2022, is \$3,290,000. The estimated total funding (direct and indirect costs) for the period of performance is \$16,370,000 to support up to six anticipated awards for Component A, up to two awards for Component B, one award for Component C, one award for Component D, and one award for Component E, for a total of up to 11 awards for the five components.

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants

Period of Performance: 5 years (7/1/2021 - 6/30/2026)

Anticipated Number of Awards: Up to six

Ceiling of Individual Award Range: \$750,000 (direct and indirect costs) (Note: the ceiling assumes the awardee will collaborate with two or more former SEED sites to contact participants and have a minimum of 2,400 eligible participants in their sample pool.)

Floor: \$230,000 (direct and indirect costs)

Estimated Average Award (Note: this average award is based on an eligible sample of 800 participants with the funding adjusted up or down based on the number of participants):

- Budget Year 1: \$425,000 (direct and indirect costs)
- Budget Years 2-5: \$405,000 (direct and indirect costs)

Estimated Total Funding: \$12,270,000 (direct and indirect costs)

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

Period of Performance: 4 years (7/1/2021 - 6/30/2025)

Anticipated Number of Awards: Up to two

Ceiling of Individual Award Range: \$20,000 (direct and indirect costs) (Year 1 only)

Floor: \$0

Estimated Average Award:

- Budget Year 1: \$20,000 (direct and indirect costs)
- Budget Year 2-4: \$160,000 (direct and indirect costs)

Estimated Total Funding: \$1,000,000 (direct and indirect costs)

Component C: Maternal Auto-Antibody Testing

Period of Performance: 3 years (7/1/2021 - 6/30/2024)

Anticipated Number of Awards: One

Ceiling of Individual Award Range: \$200,000 (direct and indirect costs)

Floor: \$0

Estimated Average Award for First Year: \$200,000 (direct and indirect costs)

Estimated Total Funding: \$600,000 (direct and indirect costs)

Component D: Genetic Analyses

Period of Performance: 5 years (7/1/2021 - 6/30/2026)

Anticipated Number of Awards: One

Ceiling of Individual Award Range: \$540,000 (direct and indirect costs) (Note: the ceiling assumes the awardee will provide secure access to high-capacity computing servers that meet Federal standards for security and confidentiality for approved SEED investigators. Applicants who are not able to provide access to high-capacity computing servers for approved investigators will receive an award closer to the average of \$450,000.)

Floor: \$0

Estimated Average Award for First Year: \$450,000 (direct and indirect costs)

Estimated Total Funding: \$2,250,000 (direct and indirect costs)

Component E: Biorepository

Period of Performance: 5 years (7/1/2021 - 6/30/2026)

Anticipated Number of Awards: One

Ceiling of Individual Award Range: \$50,000 (direct and indirect costs)

Floor: \$0

Estimated Average Award for First Year: \$50,000 (direct and indirect costs)

Estimated Total Funding: \$250,000 (direct and indirect costs)

Because the nature and scope of the proposed research will vary from application to application, it is also anticipated that the size and duration of each award may also vary. The total amount awarded, and the number of awards will depend upon the number, quality, duration, and cost of the applications received.

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

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

Award Ceiling: \$1,560,000 Per Project Period

Award Floor: \$230,000 Per Project Period

Total Period of Performance Length: 5 year(s)

Throughout the Period of Performance, CDC's commitment to continuation of awards will depend on the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports), and CDC's determination that continued funding is in the best interest of the Federal government.

HHS/CDC grants policies as described in the HHS Grants Policy Statement (<http://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf>) will apply to the applications submitted and awards made in response to this NOFO.

Section III. Eligibility Information

1. Eligible Applicants

Eligibility Category: 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
Others (see text field entitled "Additional
Information on Eligibility" for
clarification)
Unrestricted (i.e., open to any type of
entity above), subject to any clarification
in text field entitled "Additional
Information on Eligibility"

Additional Eligibility Category:

2. Foreign Organizations

Foreign Organizations are not eligible to apply.

Foreign components of U.S. Organizations are not eligible to apply.

For this announcement, applicants may not include collaborators or consultants from foreign institutions. All applicable federal laws and policies apply.

3. Additional Information on Eligibility

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

process.

Component A: Access to SEED 1-3 Participants

All applicants must document that they will have access to SEED participant's individual contact and eligibility data (i.e., status on completion of the maternal interview and clinic visit, and consent for follow-up) for all cohorts they propose to include in their recruitment pool (1, 2, and/or 3) to ensure successful completion of the SEED follow-up studies outlined in Component A of the NOFO.

Data for SEED 1-3 were collected under a Certificate of Confidentiality in accordance with section 301(d) of the Public Health Service Act. SEED 1-3 participants were provided assurances that only those entities that originally collected their personal information would use this information to contact them for future studies.

Therefore, applicants must either:

1) be the original entities that collected the original SEED data on children 2-5 years of age and their parents, and therefore have the information needed to reach these individuals for the follow-up studies;

OR

2) have established collaborative agreements to work with the entities that originally collected contact information from SEED participants (i.e., former SEED awardees) so that they can reach the SEED participants for the follow-up studies as outlined in this NOFO.

The following entities have been funded by CDC to collect data for SEED: 1) **Regents of the University of Colorado** (SEED 1-3); 2) Johns Hopkins University and Kennedy Krieger Institute (SEED 1-3); 3) Washington University (SEED 3); 4) University of North Carolina at Chapel Hill (SEED 1-3); 5) The Board of Regents at the University of Wisconsin System (SEED 3); 6) Kaiser Permanente Division of Research and the California Department of Health Services (SEED 1-2); and 7) University of Pennsylvania School of Nursing and The Children's Hospital of Pennsylvania (SEED 1-2).

To be funded for Component B, C, D, or E, applicants must apply and be funded for Component A.

4. Justification for Less than Maximum Competition

N/A

5. Responsiveness

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

Component A:

Applicants must provide written evidence they are able to access SEED participants' individual contact and eligibility data as evidenced by one of the following methods:

1. Applicants must provide evidence (e.g., notice of award for the original SEED 1, 2, or 3

studies under CDC-RFA-DD06-003, DD11-002, and/or DD16-001) that their institution was one of the original entities that collected and therefore has this information for the SEED birth cohorts they propose to follow throughout the project period.

OR

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

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

6. Required Registrations

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

- (Foreign entities only): Special Instructions for acquiring a Commercial and Governmental Entity (NCAGE) Code: <https://cage.dla.mil/>
- System for Award Management (SAM) – must maintain current registration in SAM (the replacement system for the Central Contractor Registration) to be renewed annually, <https://www.sam.gov/index.html>.
- [Grants.gov](https://www.Grants.gov)
- [eRA Commons](https://www.eRA Commons)

All applicant organizations must register with Grants.gov. Please visit www.Grants.gov at least 30 days prior to submitting your application to familiarize yourself with the registration and submission processes. The “one-time” registration process will take three to five days to complete. However, it is best to start the registration process at least two weeks prior to application submission.

All Program Directors/Principal Investigators (PD/PIs) must also work with their institutional officials to register with the eRA Commons or ensure their existing Principle Investigator (PD/PI) eRA Commons account is affiliated with the eRA commons account of the applicant organization. All registrations must be successfully completed and active before the application due date. Applicant organizations are strongly encouraged to start the eRA Commons registration process at least four (4) weeks prior to the application due date. ASSIST requires that applicant users have active eRA Commons account in order to prepare an application. It

also requires that the applicant organization's Signing Official have an active eRA Commons Signing Official account in order to initiate the submission process. During the submission process, ASSIST will prompt the Signing Official to enter their Grants.gov Authorized Organizational Representative (AOR) credentials in order to complete the submission, therefore the applicant organization must ensure that their Grants.gov AOR credentials are active.

7. Universal Identifier Requirements and System for Award Management (SAM)

All applicant organizations **must obtain** a DUN and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for Federal grants or cooperative agreements. The DUNS number is a nine-digit number assigned by Dun and Bradstreet Information Services. An AOR should be consulted to determine the appropriate number. If the organization does not have a DUNS number, an AOR should complete the [US D&B D-U-N-S Number Request Web Form](#) or contact Dun and Bradstreet by telephone directly at 1-866-705-5711 (toll-free) to obtain one. A DUNS number will be provided immediately by telephone at no charge. Note this is an organizational number. Individual Program Directors/Principal Investigators do not need to register for a DUNS number. Additionally, all applicant organizations must register in the **System for Award Management (SAM)**. Organizations must maintain the registration with current information at all times during which it has an application under consideration for funding by CDC and, if an award is made, until a final financial report is submitted or the final payment is received, whichever is later. SAM is the primary registrant database for the Federal government and is the repository into which an entity must provide information required for the conduct of business as a recipient. Additional information about registration procedures may be found at the SAM internet site at <https://www.sam.gov/index.html>. If an award is granted, the recipient organization **must** notify potential sub-recipients that no organization may receive a subaward under the grant unless the organization has provided its DUNS number to the recipient organization.

8. Eligible Individuals (Project Director/Principal Investigator) in Organizations/Institutions

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Project Director/Principal Investigator (PD/PI) is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for HHS/CDC support.

9. Cost Sharing

This FOA does not require cost sharing as defined in the HHS Grants Policy Statement (<http://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf>).

10. Number of Applications

As defined in the HHS Grants Policy Statement, (<https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf>), applications received in response to the same Notice of Funding Opportunity generally are scored individually and then ranked with other applications under peer review in their order of

relative programmatic, technical, or scientific merit. HHS/CDC will not accept any application in response to this NOFO that is essentially the same as one currently pending initial peer review unless the applicant withdraws the pending application.

Only one application per institution (normally identified by having a unique DUNS number) is allowed for each component of funding.

Section IV. Application and Submission Information

1. Address to Request Application Package

In order to use ASSIST, applicants must visit <https://public.era.nih.gov/assist> where you can login using your eRA Commons credentials, and enter the Notice of Funding Opportunity Number to initiate the application, and begin the application preparation process.

If you experience problems accessing or using ASSIST, you can refer to the ASSIST Online Help Site at: <https://era.nih.gov/erahelp/assist>. Additional support is available from the NIH eRA Service desk via:

- E-mail: <http://grants.nih.gov/support/index.html>
- Phone: 301-402-7469 or (toll-free) 1-866-504-9552. The NIH eRA Service desk is available Monday - Friday, 7 a.m. to 8 p.m. Eastern Time, excluding federal holidays.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the SF-424 (R&R) Application Guide <http://grants.nih.gov/grants/how-to-apply-application-guide.htm> and here: <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-f/general-forms-f.pdf>, except where instructed in this Notice of Funding Opportunity to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review. The package associated with this NOFO includes all applicable mandatory and optional forms. Please note that some forms marked optional in the application package are required for submission of applications for this NOFO. Follow the instructions in the SF-424 (R&R) Application Guide to ensure you complete all appropriate “optional” components. When using ASSIST, all mandatory forms will appear as separate tabs at the top of the Application Information screen; applicants may add optional forms available for the NOFO by selecting the Add Optional Form button in the left navigation panel.

3. Letter of Intent

Due Date for Letter of Intent: **10/05/2020**

Although a letter of intent is not required, is not binding, and does not enter the review of a subsequent application, the information that it contains allows CIO staff to estimate the potential review workload and plan the review.

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

- Name of the Applicant
- Descriptive title of proposed research
- Name, address, and telephone number of the PD(s)/PI(s)
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity
- Component(s) for which applicant is applying (A, B, C, D, E)

The letter of intent should be emailed to

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

4. Required and Optional Components

A complete application has many components, both required and optional. The forms package associated with this NOFO in Grants.gov includes all applicable components for this NOFO, required and optional. In ASSIST, all required and optional forms will appear as separate tabs at the top of the Application Information screen.

5. PHS 398 Research Plan Component

The SF424 (R&R) Application Guide includes instructions for applicants to complete a PHS 398 Research Plan that consists of components. Not all components of the Research Plan apply to all Notices of Funding Opportunities (NOFOs). Specifically, some of the following components are for Resubmissions or Revisions only. See the SF 424 (R&R) Application Guide <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-f/general-forms-f.pdf> and <http://grants.nih.gov/grants/how-to-apply-application-guide.htm> for additional information. Please attach applicable sections of the following Research Plan components as directed in Part 2, Section 1 (Notice of Funding Opportunity Description).

Follow the page limits stated in the SF 424 unless otherwise specified in the NOFO. As applicable to and specified in the NOFO, the application should include the bolded headers in this section and should address activities to be conducted over the course of the entire project, including but not limited to:

- 1. Introduction to Application** (for Resubmission and Revision ONLY) - provide a clear description about the purpose of the proposed research and how it addresses the specific

requirements of the NOFO.

2. Specific Aims – state the problem the proposed research addresses and how it will result in public health impact and improvements in population health.

3. Research Strategy – the research strategy should be organized under 3 headings: Significance, Innovation and Approach. Describe the proposed research plan, including staffing and time line.

4. Progress Report Publication List (for Continuation ONLY)

Other Research Plan Sections

5. Vertebrate Animals

6. Select Agent Research

7. Multiple PD/PI Leadership Plan.

8. Consortium/Contractual Arrangements

9. Letters of Support

10. Resource Sharing Plan(s)

11. Authentication of Key Biological and/or Chemical Resources

12. Appendix

All instructions in the SF424 (R&R) Application Guide <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-f/general-forms-f.pdf> and here: <http://grants.nih.gov/grants/how-to-apply-application-guide.htm> must be followed along with any additional instructions provided in the NOFO.

Applicants that plan to collect public health data must submit a Data Management Plan (DMP) in the Resource Sharing Plan section of the PHS 398 Research Plan Component of the application. A DMP is required for each collection of public health data proposed. Applicants who contend that the public health data they collect or create are not appropriate for release must justify that contention in the DMP submitted with their application for CDC funds. The DMP may be outlined in a narrative format or as a checklist but, at a minimum, should include:

- A description of the data to be collected or generated in the proposed project;
- Standards to be used for the collected or generated data;
- Mechanisms for, or limitations to, providing access to and sharing of the data (include a description of provisions for the protection of privacy, confidentiality, security, intellectual property, or other rights - this section should address access to identifiable and de-identified data);
- Statement of the use of data standards that ensure all released data have appropriate documentation that describes the method of collection, what the data represent, and potential limitations for use; and
- Plans for archiving and long-term preservation of the data, or explaining why long-term preservation and access are not justified (this section should address archiving and preservation of identifiable and deidentified

data).

Examples of DMPs may be found here: USGS, <http://www.usgs.gov/products/data-and-tools/data-management/data-management-plans>

The applicant's research plan should address activities that will be conducted over the entire period of performance and should include the following items:

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Surveys of Existing SEED Participants

5-year Period of Performance: 7/1/2021 - 6/30/2026

Expertise

Describe experience in

1. ASD and developmental disability research, including ability to address priority topics, produce high-quality outputs (e.g., publications in high-impact journals, presentation at high-profile meetings), and impact public health programs and policies. Include evidence of expertise in epidemiology, maternal and child health, public health, developmental disabilities, and biostatistics, and any specialty area (child psychiatry, clinical psychology, developmental psychology, pediatric medicine). Detail expertise available in pediatric medicine.
2. Developing survey instruments and prioritizing the use of standardized questions among respondents in multiple populations or multiple sites.
3. Implementing epidemiologic follow-up studies and other relevant epidemiologic or psychometric research studies, including:
 - a. Scope, complexity and size (including final sample size) of previous studies;
 - b. Measures of implementation success from previous studies (e.g., research recruitment and enrollment rates; study completion rates);
 - c. Methods for conducting research involving parents and their adult child with ASD or other developmental disabilities (e.g., methods for obtaining consent from both parents and the adult child, conducting interviews with adults with ASD or other developmental disabilities).

Capacity and Approach

Partnerships and Collaborations

Describe experience in

1. Participating in and taking on leadership roles in multi-site collaborative research programs, including evidence of participation in workgroups, conference calls and in-person meetings.
2. Adhering to standard protocols, data collection, and data management for multi-site collaborative research programs.
3. Maintaining confidentiality and privacy of participants and adhering to all provisions of the SEED Certificate of Confidentiality.
4. Contributing to a shared pool of de-identified data and common data sharing guidelines for analysis, presentation, publication, data release, and data return.

5. Obtaining and maintaining IRB approval and adhering to rules for protection of human subjects.

Recruitment Pool

1. Provide the estimated number of SEED participants from phase 1, 2, and/or 3 available for potential inclusion in a follow-up survey. Provide estimates based on criteria as follows:
 - a. Child received a final classification of ASD, developmental disability (DD), or population control (POP) in SEED 1, 2 or 3;
 - b. Child's primary caregiver consented for future studies;
 - c. Caregiver and child completed the following data collection components:
 - i. Maternal (caregiver) Interview;
 - ii. Clinic visit (Mullen and, if applicable, Vineland, ADOS, and ADI-R).
2. Describe the demographic feature of potential applicant pool, including diversity by race-ethnicity.
3. Applicants may collaborate with former SEED sites to maximize the number of former SEED participants included in the potential recruitment pool. All new sites and former SEED sites proposing to include former SEED 1, 2 or 3 participants from sites other than their own should provide documentation (e.g., a subcontract or a memorandum of understanding) of the ability to access identifiable contact information (names, addresses, phone numbers, etc.) collected by another SEED site.

Participant Tracing

Describe capacity to

1. Provide contact information for former SEED participants and work with the central interviewing contractor to obtain the most current contact information; include strategies and plans to successfully reach through mailings and/or other approaches and confirm contact with no less than 90% of participants deemed eligible for inclusion.
2. Collaborate with the central interviewing contractor to develop and enter participant contact information into centralized tracking system.
3. Maintain confidentiality and privacy of participants and adhere to all provisions of the SEED Certificate of Confidentiality.

Participant Enrollment and Retention

Describe capacity and planned approach to

1. Conduct pre-consent calls (if required to share participant information) or provide information to support the central interviewing contractor in obtaining no less than a 75% enrollment rate among participants successfully traced.
2. Respond to participant inquiries.
3. Enroll and retain participants, including ability to support the central interviewing contractor in achieving no less than a 40% completion rate for the second follow-up surveys of SEED 1 participants (parent and adult child). Include experience implementing community outreach and participant retention and satisfaction strategies

(e.g., social networking, a bi-annual newsletter to SEED participants to boost awareness and interest).

4. Retain diversity of participants by race-ethnicity.

Management and Staffing

Provide a clear management and staffing plan to support all Component A activities. Roles should be closely linked with project objectives and anticipated outcomes and should reflect the unique role each partner will play, including

1. Document (with curriculum vitae) and describe experience and expertise of proposed staff including the project leadership as indicated in 2-5 below.
2. Study Planning
 - a. During 7/1/2021 - 6/30/2022, a minimum 25% effort is expected from the PI or co-investigators in combination for developing the study protocol and assessment tools, collaborating with CDC to obtain IRB approval and updating the SEED analysis and publication guidelines.
 - b. Collectively, the PI and co-investigators should demonstrate expertise in epidemiology, maternal and child health, public health, developmental disabilities, and biostatistics, as well as at least one specialty area in child psychiatry, clinical psychology, developmental psychology, pediatric medicine, or genetics. Although expertise in only one specialty area is required, a variety of expertise in specialty areas is desired, in particular, expertise in pediatric medicine.
3. Data Analysis and Establishment of Analytic Priorities
 - a. During 07/01/2022-06/30/2026 a minimum of 10% effort is expected from the PI or co-investigators in combination for ongoing assessment of analytic priorities, and analysis planning.
 - b. During the entire 5-year period of performance the equivalent of 1 FTE at 100% effort is required with sufficient training and experience (e.g., postdoctoral fellow) to support data coding and analysis, data documentation and manuscript preparation.
 - c. Describe your previous experience and plans for participation in workgroups to establish a library of investigator derived variables.
 - d. Describe your ability and willingness to support SEED data management, analysis, and reporting plans.
4. Study Implementation. Provide a detailed description and site-specific plan for implementing SEED data collection, including a staffing plan describing who will perform the following duties:
 - a. Working with the central interviewing contractor;
 - b. Compiling lists and contact information for SEED participants eligible for the follow-up studies;
 - c. Conducting contact tracing in collaboration with the central interviewing contractor;
 - d. Sending out initial invitation letters/packets to all eligible participants;
 - e. Conducting invitation/enrollment calls or regularly communicating with the central interviewing contractor about eligible participants sent study materials;

- f. Providing additional demographic data that may assist the central interviewing contractor with locating/identifying current contact information for eligible families/participants;
 - g. Communicating and addressing questions as they arise from interested and enrolled participants;
 - h. Collaborating with CDC to maintain IRB approval and ensuring staff meet educational program requirements for protection of human subjects.
5. Study Evaluation. Provide a detailed description for who will develop and implement the evaluation plan, including their experience and expertise in evaluation.
 6. Describe plans for maintaining project activities when staff vacancies occur.

Timeline

1. Provide a timeline for key milestones and project development activities to occur in the first 12 months of the five-year project. Include milestones that will be used to demonstrate progress toward collaborating with CDC and providing documentation for CDC to obtain IRB approval and completing development of the analysis, evaluation, and translation plans.
2. Identify key milestones for the remainder of the period of performance.

Budget

1. Provide a detailed budget and line-item justification of all operating expenses that are consistent with the planned activities of the project. In addition to staffing, include
 - a. Tracing and recruitment support costs (e.g., contact tracing, community outreach, printing study materials, including invitation response cards/letters, mailing costs/postage, photocopying, staffing for invitation/enrollment calls as relevant, etc.) in line with the size of the recruitment pool of former SEED participants.
 - b. Travel support: proposed budget to include funds for at least one person to attend an annual SEED in-person meeting in Atlanta.
 - c. Equipment: Laptops/encrypted thumb drives/software and related IT needs.
 - d. Facility costs (rent, electricity, etc.).

Component B: In-person Assessment of Intellectual Abilities of SEED Participants

4-year Period of Performance: 7/1/2021 - 6/30/2025

Expertise

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

1. ASD and developmental disability research related to psychometric measurements, including ability to produce high-quality outputs (e.g., publications in peer-reviewed journals, presentation at high-profile meetings), and impact public health programs and policies.
2. Conducting assessments of participants in large-scale research studies, and ability to successfully plan and implement Component B objectives outlined in this NOFO, including

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

Capacity and Approach

Describe capacity to

1. Maximize participation and achieve the target of no less than 100 completed in-person assessments, including participants of diverse race-ethnicity:
 - a. Demonstrate sufficient recruitment pool of former SEED participants, under the assumption that 57% of families in the recruitment pool will complete the first follow-up survey and that 40% of those in the ASD and DD arms who complete the first follow-up survey will continue to complete the in-person assessment.
 - b. Methods for promoting interest among and enrollment of diverse participants;
 - c. Methods to schedule eligible participants, including all approaches to maximize the number of visits scheduled;
 - d. Active follow-up of families who were scheduled for an in-person visit but did not complete the visit for any reason; and
 - e. Dedicated staff supported by the project to implement these procedures.
2. Conduct in-person assessments of SEED participants including your
 - a. Ability to purchase and secure psychological testing kits and manuals;
 - b. In-person assessment visit locations (e.g., clinic site), with details outlining
 - i. Security, privacy, accessibility, furniture, and lighting; and
 - ii. Access to and from public transportation sources.
3. Ability to adhere to standard protocols, data collection, and data management for multi-site collaborative research programs.

Management and Staffing

1. Provide a clear management and staffing plan to support all Component B activities. Minimum staffing should include
 - a. A supervising site clinician who meets the following criteria: (1) a doctorate degree in counseling, education, occupational therapy, speech-language pathology, psychology, social work, or related field; OR a master's degree in the fields listed and a license or certification to practice in that field with; (2) at least 5 years of experience with the administration and interpretation of psychological test results; (3) previous experience administering psychological tests to individuals with developmental disabilities, (4) previous experience supervising psychometrists or other clinical staff; and (5) previous experience delivering feedback to families about the developmental status of their child.
 - b. A psychometrist who meets the following criteria: (1) at least a Master's degree in counseling, education, occupational therapy, speech-language pathology, psychology, social work, or related field; OR a bachelor's degree in the fields

listed and a license or certification to practice in that field with; (2) at least one year experience with administration/interpretation of psychological test results; and (3) previous experience administering psychological tests to individuals with developmental disabilities.

Note that the supervising site clinician can also serve as the psychometrist.

2. If the applicant proposes to include Spanish-speaking participants, describe the resources and staff expertise necessary to conduct the in-person assessment in Spanish.

Budget

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

1. Equipment, such as testing kits, and storage;
2. Rental costs for clinic locations, if needed;
3. Personnel costs, including salary and travel costs to and from the visit location(s);
4. Participant mailings and incentives; and
5. Miscellaneous (e.g., materials such as water and snacks to ensure participant comfort at the in-person visit).

Component C: Maternal Auto-Antibody Testing

3-year Period of performance: 7/1/2021 - 6/30/2024

Expertise

Provide evidence (curriculum vitae) and describe your experience and expertise in ASD and developmental disability research related to immune correlates of neurodevelopmental disorders, including your ability to produce high-quality outputs (e.g., publications in peer-reviewed journals, presentation at high-profile meetings) and impact public health programs and policies.

Capacity and Approach

1. Provide evidence of expertise in conducting auto-antibody assays, including expertise in selection of most appropriate assays and methods and oversight of laboratory procedures including, but not limited to, transport, storage, and analysis of specimens, and quality assurance procedures.
2. Provide a plan for formulating analytic priorities, conducting statistical analysis and reporting of results and willingness/ability to collaborate with CDC and other study sites.

Management and Staffing

Provide a clear management and staffing plan to support all Component C activities, including selection and development of assay protocols, oversight of project and laboratory activities, development of analytic priorities, and data analysis and presentation of results.

Budget

Provide a detailed budget and line-item justification of all operating expenses that are consistent

with the planned activities to include costs for

1. Assay materials
2. Technician
3. Project Management
4. Use of laboratory space and equipment
5. Programmer/Analysts
6. Oversight by Principal Investigator

Component D: Genetic Analyses

5-year Period of Performance: 7/1/2021 - 6/30/2026

Expertise

Provide evidence (with curriculum vitae) of professional reports, publications, and presentations that illustrate your ability to successfully identify and evaluate the highest priority analyses related to the genetics of ASD and how environments, behaviors, genetic variation, and epigenetic variation contribute to risk for ASD and other related neurodevelopmental and psychiatric disorders. Include evidence of your ability to produce high-quality outputs (e.g., publications in peer review journals, presentation at high-profile meetings), and impact public health programs and policies.

Capacity and Approach

Collaboration/Contribution to Data Repositories

1. Describe your expertise and experience in contributing to and using data from biological data repositories, such as the National Database for Autism Research (NDAR) and the database of Genotypes and Phenotypes (dbGaP).
2. Describe your expertise and experience in contributing data for meta-analyses and replication data sets.

Development of High-throughput Genomic Approaches

1. Describe your expertise in methodological developments for genetic epidemiology studies.
2. Describe your experience with pipeline development and controlling for batch effects.

Analytic Support

1. Describe your expertise in epidemiology, statistical genetics, and management of large data sets.
2. Describe your experience in developing measures and providing analytic support for copy number variant (CNV), single nucleotide polymorphism (SNP) and polygenic risk score (PRS) level analyses.
3. Describe your capacity to ensure appropriate institutional computing resources that meet Federal standards for security and protection of confidentiality, and experience with maintaining security measures.
4. Describe your capacity to provide SEED investigators access to these resources through

a platform that meets Federal standards for security and protection of confidentiality.

Management and Staffing

Provide a detailed management and staffing plan for the applicant, including percent effort for the PI and co-investigators, genetic biostatisticians, analysis and postdoctoral fellows and laboratory management staff. Minimum effort should include 1 full-time genetic biostatistician, 1 full-time data analyst with doctoral level training, and 10% of PI or co-investigator effort.

Budget

Provide a detailed line-item budget, including costs for salary support, and costs for providing access to high-power computing that meets Federal standards for security and confidentiality.

Component E: Biorepository

5-year Period of performance: 7/1/2021 - 6/30/2026

1. Describe your experience and ability to successfully serve as the SEED Central Laboratory and Biospecimen Repository and support SEED scientific goals, including long-term storage, tracking and retrieval of samples.
2. Describe your ability and approach for maintaining confidentiality and privacy of all participant biospecimen data.
3. Provide a detailed budget and line-item justification for all staffing, equipment and operating expenditures.

6. Appendix

Do not use the appendix to circumvent page limits. A maximum of 10 PDF documents are allowed in the appendix. Additionally, up to 3 publications may be included that are not publically available. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

7. Page Limitations

All page limitations described in this individual NOFO must be followed. For this specific NOFO, the Research Strategy component of the Research Plan narrative is limited to 25 pages. Supporting materials for the Research Plan narrative included as appendices may not exceed 10 PDF files with a maximum of 50 pages for all appendices. Pages that exceed page limits described in this NOFO will be removed and not forwarded for peer review, potentially affecting an application's score.

8. Format for Attachments

Designed to maximize system-conducted validations, multiple separate attachments are required for a complete application. When the application is received by the agency, all submitted forms and all separate attachments are combined into a single document that is used by peer reviewers and agency staff. Applicants should ensure that all attachments are uploaded to the system.

CDC requires all text attachments to the Adobe application forms be submitted

as PDFs and that all text attachments conform to the agency-specific formatting requirements noted in the SF424 (R&R) Application Guide <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-f/general-forms-f.pdf>.

9. Submission Dates & Times

Part I. Overview Information contains information about Key Dates. Applicants are strongly encouraged to allocate additional time and submit in advance of the deadline to ensure they have time to make any corrections that might be necessary for successful submission. This includes the time necessary to complete the application resubmission process that may be necessary, if errors are identified during validation by Grants.gov and the NIH eRA systems. The application package is not complete until it has passed the Grants.gov and NIH eRA Commons submission and validation processes.

Organizations must submit applications using the ASSIST web-based application preparation and submission process.

ASSIST will validate applications before submission. If the system detects errors, then the applicant must correct errors before their application can be submitted.

Applicants are responsible for viewing their application in ASSIST after submission to ensure accurate and successful submission through Grants.gov. If the submission is not successful and post-submission errors are found, then those errors must be corrected and the application resubmitted in ASSIST.

Applicants are able to access, view, and track the status of their applications in the eRA Commons.

Information on the submission process is provided in the SF-424 (R&R) Application Guidance and ASSIST User Guide at https://era.nih.gov/files/ASSIST_user_guide.pdf.

Note: HHS/CDC grant submission procedures do not provide a grace period beyond the grant application due date time to correct any error or warning notices of noncompliance with application instructions that are identified by Grants.gov or eRA systems (i.e. error correction window).

Applicants who encounter problems when submitting their applications must attempt to resolve them by contacting the NIH eRA Service desk at:

Toll-free: 1-866-504-9552; Phone: 301-402-7469

<http://grants.nih.gov/support/index.html>

Hours: Mon-Fri, 7 a.m. to 8 p.m. Eastern Time (closed on federal holidays)

Problems with Grants.gov can be resolved by contacting the Grants.gov Contact Center at:

Toll-free: 1-800-518-4726

<https://www.grants.gov/web/grants/support.html>

support@grants.gov

Hours: 24 hours a day, 7 days a week; closed on Federal holidays

It is important that applicants complete the application submission process well in advance of the due date time.

After submission of your application package, applicants will receive a "submission receipt" email generated by Grants.gov. Grants.gov will then generate a second e-mail message to applicants which will either validate or reject their submitted application

package. A third and final e-mail message is generated once the applicant's application package has passed validation and the grantor agency has confirmed receipt of the application.

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

1. Track submission and verify the submission status (tracking should be done initially regardless of rejection or success).
 - a. If the status states "rejected," be sure to save time stamped, documented rejection notices, and do #2a or #2b
2. Check emails from both Grants.gov and NIH eRA Commons for rejection notices.
 - a. If the deadline has passed, he/she should email the Grants Management contact listed in the Agency Contacts section of this announcement explaining why the submission failed.
 - b. If there is time before the deadline, correct the problem(s) and resubmit as soon as possible.

Due Date for Applications: **11/10/2020**

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](#).

11. Funding Restrictions

Expanded Authority:

For more information on expanded authority and pre-award costs, go to <https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf> and speak to your GMS.

All HHS/CDC awards are subject to the federal regulations, 45 CFR 75, terms and conditions, and other requirements described in the HHS Grants Policy Statement. Pre-award costs may be allowable as an expanded authority, but only if authorized by CDC.

Protecting Life in Global Health Assistance:

In accordance with the United States Protecting Life in Global Health Assistance policy, all non-governmental organization (NGO) applicants acknowledge that foreign NGOs that receive funds provided through this award, either as a prime recipient or subrecipient, are strictly prohibited, regardless of the source of funds, from performing abortions as a method of family planning or engaging in any activity that promotes abortion as a method of family planning, or to provide financial support to any other foreign non-governmental organization that conducts such activities. See Additional Requirement (AR) 35 for applicability (<https://www.cdc.gov/grants/additional-requirements/ar-35.html>).

Public Health Data:

CDC requires that mechanisms for, and cost of, public health data sharing be included in grants, cooperative agreements, and contracts. The cost of sharing or archiving public health data may also be included as part of the total budget requested for first-time or continuation awards.

Data Management Plan:

Fulfilling the data-sharing requirement must be documented in a Data Management Plan (DMP) that is developed during the project planning phase prior to the initiation of generating or collecting public health data and must be included in the Resource Sharing Plan(s) section of the PHS398 Research Plan Component of the application.

Applicants who contend that the public health data they collect or create are not appropriate for release must justify that contention in the DMP submitted with their application for CDC funds (for example, privacy and confidentiality considerations, embargo issues).

Recipients who fail to release public health data in a timely fashion will be subject to procedures normally used to address lack of compliance (for example, reduction in funding, restriction of funds, or award termination) consistent with 45 CFR 74.62 or other authorities as appropriate. For further information, please see: <https://www.cdc.gov/grants/additional-requirements/ar-25.html> for revised AR-25.

Human Subjects:

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

If the proposed research project involves more than one institution and will be conducted in the United States, awardees are expected to use a single Institutional Review Board (sIRB) to conduct the ethical review required by HHS regulations for the Protections of Human Subjects Research, and include a single IRB plan in the application, unless review by a sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy or a compelling justification based on ethical or human subjects protection issues or other well-justified reasons is provided. Exceptions will be reviewed and approved by CDC in accordance with Department of Health and Human Services (DHHS) Regulations (Title 45 Code of Federal Regulations Part 46), or a restriction may be placed on the award. For more information, please contact the scientific/research contact included on this NOFO.

Note: The sIRB requirement applies to participating sites in the United States. Foreign sites participating in CDC-funded, cooperative research studies are not expected to follow the requirement for sIRB.

12. Other Submission Requirements and Information**Risk Assessment Questionnaire Requirement**

CDC is required to conduct pre-award risk assessments to determine the risk an applicant poses

to meeting federal programmatic and administrative requirements by taking into account issues such as financial instability, insufficient management systems, non-compliance with award conditions, the charging of unallowable costs, and inexperience. The risk assessment will include an evaluation of the applicant's CDC Risk Questionnaire, located at <https://www.cdc.gov/grants/documents/PPMR-G-CDC-Risk-Questionnaire.pdf>, as well as a review of the applicant's history in all available systems; including OMB-designated repositories of government-wide eligibility and financial integrity systems (see 45 CFR 75.205(a)), and other sources of historical information. These systems include, but are not limited to: FAPIIS (<https://www.fapiis.gov/>), including past performance on federal contracts as per Duncan Hunter National Defense Authorization Act of 2009; Do Not Pay list; and System for Award Management (SAM) exclusions.

CDC requires all applicants to complete the Risk Questionnaire, OMB Control Number 0920-1132 annually. This questionnaire, which is located at <https://www.cdc.gov/grants/documents/PPMR-G-CDC-Risk-Questionnaire.pdf>, along with supporting documentation must be submitted with your application by the closing date of the Notice of Funding Opportunity Announcement. Upload the questionnaire and supporting documents as an attachment in the "12. Other Attachments" section of the "RESEARCH & RELATED Other Project Information" section of the application. If your organization has completed CDC's Risk Questionnaire within the past 12 months of the closing date of this NOFO, then you must submit a copy of that questionnaire, or submit a letter signed by the authorized organization representative to include the original submission date, organization's EIN and DUNS.

When uploading supporting documentation for the Risk Questionnaire into this application package, clearly label the documents for easy identification of the type of documentation. For example, a copy of Procurement policy submitted in response to the questionnaire may be labeled using the following format: Risk Questionnaire Supporting Documents _ Procurement Policy.

Duplication of Efforts

Applicants are responsible for reporting if this application will result in programmatic, budgetary, or commitment overlap with another application or award (i.e. grant, cooperative agreement, or contract) submitted to another funding source in the same fiscal year.

Programmatic overlap occurs when (1) substantially the same project is proposed in more than one application or is submitted to two or more funding sources for review and funding consideration or (2) a specific objective and the project design for accomplishing the objective are the same or closely related in two or more applications or awards, regardless of the funding source. Budgetary overlap occurs when duplicate or equivalent budgetary items (e.g., equipment, salaries) are requested in an application but already are provided by another source. Commitment overlap occurs when an individual's time commitment exceeds 100 percent, whether or not salary support is requested in the application. Overlap, whether programmatic, budgetary, or commitment of an individual's effort greater than 100 percent, is not permitted. Any overlap will be resolved by the CDC with the applicant and the PD/PI prior to award.

Report Submission: The applicant must upload the report under "Other Attachment Forms." The document should be labeled: "Report on Programmatic, Budgetary, and Commitment

Overlap.”

Application Submission

Applications must be submitted electronically following the instructions described in the SF 424 (R&R) Application Guide. **PAPER APPLICATIONS WILL NOT BE ACCEPTED.**

Applicants must complete all required registrations before the application due date. Section III.6 "Required Registrations" contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically (<https://grants.nih.gov/grants/how-to-apply-application-guide.html>).

Important reminders:

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

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

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

See more resources to avoid common errors and submitting, tracking, and viewing applications:

- http://grants.nih.gov/grants/ElectronicReceipt/avoiding_errors.htm
- http://grants.nih.gov/grants/ElectronicReceipt/submit_app.htm
- https://era.nih.gov/files/ASSIST_user_guide.pdf
- <http://era.nih.gov/erahelp/ASSIST/>

Upon receipt, applications will be evaluated for completeness by the CDC Office of Grants Services (OGS) and responsiveness by OGS and the Center, Institute or Office of the CDC. Applications that are incomplete and/or nonresponsive will not be reviewed.

Section V. Application Review Information

1. Criteria

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

Overall Impact

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

Scored Review Criteria

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

Significance

Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Components A-D:

- Does the applicant articulate how their involvement in the study will address a problem of great importance to public health research and/or practice?
- Does the applicant specify how the study could lead to future investigations and/or open new areas of research, and how they could contribute to these future activities?
- Does the applicant describe how they are positioned to communicate the significance of this work to a variety of stakeholders?

Investigator(s)

Are the PD/PIs, collaborators, and other researchers well suited to the project? Have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

Component A: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Studies of Existing SEED Participants

- Do the investigators have a successful track record in ASD and developmental disability research, including a record of publication in high-impact journals, and evidence of research results contributing toward improvements in public health?
- Has the applicant provided solid evidence for successful implementation and completion of research studies, particularly studies involving longitudinal follow-up?
- Do the PI and co-investigators in combination demonstrate expertise in epidemiology, maternal and child health, public health, developmental disabilities, and biostatistics, as well as at least one specialty area in child psychiatry, clinical psychology, developmental psychology, pediatric medicine, or genetics? Although expertise in only one specialty area is required, a variety of expertise in specialty areas is desired, in particular, expertise in pediatric medicine.
- Is there at least 25% PI or co-investigator effort in combination in year 1 of the period of performance and 10% in subsequent years of the study?
- Is there an equivalent of 1 FTE with 100% effort with enough training and experience to support data coding and analysis, data documentation, and manuscript preparation?
- Has sufficient project coordination staff been identified to complete the mailings and participant recruitment in a timely manner?
- Is there evidence of previous successful collaboration with CDC and across sites and institutions on the implementation of multi-site research studies?
- Has the applicant demonstrated willingness and ability to assume active participation in the identification of research gaps and priority analyses for existing SEED data?
- Has the applicant demonstrated willingness and ability to assume active participation in the development of the follow-up study protocol that includes the CDC parameters described in this NOFO and to actively participate in committees/workgroups and meetings with CDC, contractors, and other Component A awardees?

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

- Do the investigators have a successful track record of high-quality outputs (as evidence by publications in high impact journals) and contributions to improvements in public health practice and population health?
- Does the applicant have a track record in psychometric assessment?
- Has the applicant provided evidence for successful implementation of in-person assessments, in particular those involving individuals with developmental disabilities?
- Does the investigator have expertise in psychological test administration and interpretation?
- Has the applicant provided a detailed staffing and resources plan, including a description of staff time commitments and necessary expertise of staff in critical areas of implementation (i.e., clinical supervision and psychometric assessment)?
- Has the applicant demonstrated willingness to participate in a workgroup to identify data collection instruments to be administered during the in-person visit?
- Has the applicant demonstrated willingness to participate in on-going clinical workgroup meetings to discuss study implementation and progress?

Component C: Maternal Auto-Antibody Testing

- Do the investigators have a successful track record of high-quality outputs (as evidence by publications in high impact journals) and contributions to improvements in public health practice and population health?
- Do the investigators have a successful track record in immunology research?
- Have the investigators demonstrated the laboratory expertise to run autoantibody assays, including selection of most appropriate test, methods and quality control?
- Is there evidence of past collaborations among investigators of the proposed research team?

Component D: Genetic Analyses

- Have previous research results provided high-quality outputs (as evidence by publications in high impact journals) and contributed to improvements in public health practice and population health?
- Do the investigators have a successful track record in genetics, genetic epidemiology and investigation of genetic and gene by environment determinants of ASD or related neurodevelopmental and psychiatric disorders?
- Does the applicant have a track record of collaboration with ASD researchers with expertise in genetics and pooling data for meta-analyses and contribution to biorepositories?
- Does the staffing plan include a full-time genetic biostatistician and doctoral level data analysis? Is there a commitment for 10% effort from the PI and/or co-investigators?
- Does the applicant have experience in pipeline development for genetic data, including controlling for batch effects and implementation of quality control measures?
- Does the applicant have experience providing analytic support for genetic analyses?

Component E: Biorepository

- Has the applicant provided evidence of experience for successful maintenance of a central biorepository, including secure sample preservation and efficient tracking and retrieval of bio samples?

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: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Studies of Existing SEED Participants

- Do the proposed methods build on previous experience with ASD research and provide a high likelihood of success in identifying new modifiable risk factors?
- Do the proposed methods build on previous experience with ASD research and provide

a high likelihood of success in expanding our understanding of the health and functional outcomes of individuals identified in early childhood with ASD across their lifespan and what factors may improve these outcomes.

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

- Do the proposed methods build on previous experience with ASD research and provide a high likelihood of success in enhancing our understanding of the gap between intellectual ability and daily living skills to inform policies on eligibility for services?

Component C: Maternal Auto-Antibody Testing

- Do the proposed methods build on previous experience with research on maternal autoantibodies as associated with ASD and provide a high likelihood of success in identifying how maternal immune regulation may be involved in neurodevelopment.

Component D: Genetic Analyses

- Do the proposed methods build on previous experience with ASD research and provide a high likelihood of success in identifying new modifiable genetic risk factors?

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: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Studies of Existing SEED Participants

- Does the applicant provide well-reasoned and detailed rationale for developing analyses and establishing analytic priorities for ASD research?
- Does the applicant consider the priority objectives outline by the Interagency Autism Coordinating Committee Strategic Plan (<https://iacc.hhs.gov/publications/strategic-plan/2017/>) or by other ASD research stakeholder groups in establishing analytic priorities?
- If proposing accessing another SEED site's participants, does the applicant provide evidence of the ability to access the necessary individual contact information necessary to contact participants for follow-up?
- Does the applicant have a robust plan for tracing contact information and contacting or supporting the central interviewing contractor to reach no less than 90% of eligible SEED participants?

- Does the applicant have a robust plan for working collaboratively with the central interviewing contractor to enroll no less than 75% eligible SEED participants successfully contacted?
- Does the applicant have a robust plan for retaining participants once enrolled and supporting the central interviewing contractor to conduct a second follow-up survey (parent and adult child) among no less than 40% of SEED 1 families who completed the first follow-up survey?
- Does the plan include strategies to reach and retain participants of diverse demographic characteristics, including race-ethnicity?
- Are the resources outlined by the applicant in line with the size of participant recruitment pool and need for tracing, contacting and retaining participants for the follow-up surveys?
- Has the applicant provided a high-quality plan for communication of study progress and results to the community, local partners, and participants?
- Has the applicant demonstrated the willingness and ability to carry out SEED quality control, data security protocols, and data management protocols in collaboration with a central interviewing contractor?

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

- How large of a recruitment pool of eligible participants can the applicant access?
- Has the applicant demonstrated the ability to complete a minimum of 100 in-person assessments?
- Has the applicant described procedures to maximize retention and participation, including active follow-up of families who were scheduled for an in-person visit but did not complete the visit for any reason, and strategies to reach and retain participants of diverse demographic characteristics, including race-ethnicity?
- If the applicant proposes to include Spanish-speaking participants, do they have resources and staff expertise necessary to conduct the research in Spanish?
- Has the applicant demonstrated willingness to conduct quality control activities for psychometric assessments?
- Has the applicant outlined data confidentiality and security procedures, including storage of psychometric assessment test results?

Component C: Maternal Auto-Antibody Testing

- Does the applicant have a plan in place to select appropriate assays, methods, and quality control measures?
- Does the applicant provide well-reasoned and detailed rationale for developing analyses and establishing analytic priorities?

Component D: Genetic Analyses

- Does the applicant have a detailed plan to prepare for the expert workgroup meetings to establish an analytic agenda and priorities for use of SEED biospecimens?
- Does the applicant have a well-thought-out action plan for establishing collaborations

- with ASD researchers to conduct further genetic testing of SEED biospecimens?
- Does the applicant describe plans for processing, quality control and pipeline development for newly generated genetic data from SEED biospecimens?
- Does the application have an effective plan for providing analytic support for genetic data processing and variable development for use in genetic analyses?
- Does the applicant describe plans for providing secure access to high-capacity computing servers that meet Federal standards for security and confidentiality for approved SEED investigators?

Component E: Biorepository

- Has the applicant demonstrated a high-quality plan for implementing the SEED Central Biorepository, including tracking, accounting and retrieval procedures, and contingency plans should the applicant become unable to maintain the SEED Biorepository?

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: Enhanced Epidemiologic Research Using Existing SEED Data and Follow-up Studies of Existing SEED Participants

- Will the project benefit from unique features of the scientific environment or collaborative arrangements, such as a collaboration between an academic center and a health department or research centers?
- Does the applicant show capacity for establishing inter-institutional collaborations?

Component B: In-Person Assessment of Intellectual Abilities of SEED Participants

- Has the applicant provided evidence for access to clinical space (potentially at multiple locations) to reasonably accommodate participants, or provided feasible non-clinic alternatives (e.g., home visits)? Is it accessible to and from public transportation sources?
- Does the proposed clinic space and/or non-clinic alternatives offer sufficient availability to support the expected participant volume with timely and flexible scheduling?
- Does the proposed clinic space and/or non-clinic alternatives have adequate security, privacy, accessibility, furniture, and lighting?

Component C: Maternal Auto-Antibody Testing

- Does the applicant have the laboratory facilities to carry out the proposed auto-antibody assays?

Component D: Genetic Analyses

- Can the applicant provide access to high-power computing capacity and data storage for SEED investigators that meets Federal standards for security and confidentiality?

Component E: Biorepository

- Has the applicant provided evidence for high-quality biospecimen repository facilities and staff expertise?

2. Additional Review Criteria

As applicable for the project proposed, *reviewers will evaluate* the following additional items while determining scientific and technical merit, and in providing an overall impact/priority score, but *will not give separate scores* for these items.

Protections for Human Subjects

If the research involves human subjects but does not involve one of the six categories of research that are exempt under [45 CFR Part 46](#), the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the HHS/CDC Requirements under AR-1 Human Subjects Requirements (<https://www.cdc.gov/grants/additionalrequirements/ar-1.html>).

If your proposed research involves the use of human data and/or biological specimens, you must provide a justification for your claim that no human subjects are involved in the Protection of Human Subjects section of the Research Plan.

Inclusion of Women, Minorities, and Children

When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children. For additional information on review of the Inclusion section, please refer to the policy on the Inclusion of Women and Racial and Ethnic Minorities in Research (https://www.cdc.gov/maso/Policy/Policy_women.pdf) and the policy on the Inclusion of Persons Under 21 in Research (<https://www.cdc.gov/maso/Policy/policy496.pdf>).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following four points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) procedures for limiting discomfort,

distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 4) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (<https://olaw.nih.gov/guidance/vertebrate-animal-section.htm>).

Biohazards

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

Dual Use Research of Concern

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

For more information about this Policy and other policies regarding dual use research of concern, visit the U.S. Government Science, Safety, Security (S3) website at: <http://www.phe.gov/s3/dualuse>. Tools and guidance for assessing DURC potential may be found at: <http://www.phe.gov/s3/dualuse/Pages/companion-guide.aspx>.

3. Additional Review Considerations

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

Awardees will implement a standard SEED Data Management Plan established by CDC and the central interviewing contractor in accordance with Federal data sharing requirements. The Data Management Plan will be provided to recipients following award.

Resource Sharing Plan(s)

HHS/CDC policy requires that recipients of grant awards make research resources and data readily available for research purposes to qualified individuals within the scientific community after publication. Please see: <https://www.cdc.gov/grants/additionalrequirements/ar-25.html>

New additional requirement: CDC requires recipients for projects and programs that involve data collection or generation of data with federal funds to develop and submit a Data Management Plan (DMP) for each collection of public health data.

Investigators responding to this Notice of Funding Opportunity should include a detailed DMP in the Resource Sharing Plan(s) section of the PHS 398 Research Plan Component of the application. The [AR-25](#) outlines the components of a DMP and provides

additional information for investigators regarding the requirements for data accessibility, storage, and preservation.

The DMP should be developed during the project planning phase prior to the initiation of collecting or generating public health data and will be submitted with the application. The submitted DMP will be evaluated for completeness and quality at the time of submission.

The DMP should include, at a minimum, a description of the following:

- A description of the data to be collected or generated in the proposed project;
- Standards to be used for the collected or generated data;
- Mechanisms for, or limitations to, providing access to and sharing of the data (include a description of provisions for the protection of privacy, confidentiality, security, intellectual property, or other rights - this section should address access to identifiable and de-identified data);
- Statement of the use of data standards that ensure all released data have appropriate documentation that describes the method of collection, what the data represent, and potential limitations for use; and
- Plans for archiving and long-term preservation of the data, or explaining why long-term preservation and access are not justified (this section should address archiving and preservation of identifiable and de-identified data).

Applications submitted without the required DMP may be deemed ineligible for award unless submission of DMP is deferred to a later period depending on the type of award, in which case, funding restrictions may be imposed pending submission and evaluation.

Budget and Period of Support

Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research. The applicant can obtain guidance for completing a detailed justified budget on the CDC website, at the following Internet address: <http://www.cdc.gov/grants/interestedinapplying/applicationresources.html>

The budget can include both direct costs and indirect costs as allowed.

Indirect costs could include the cost of collecting, managing, sharing and preserving data.

Indirect costs on grants awarded to foreign organizations and foreign public entities and performed fully outside of the territorial limits of the U.S. may be paid to support the costs of compliance with federal requirements at a fixed rate of eight percent of modified total direct costs exclusive of tuition and related fees, direct expenditures for equipment, and subawards in excess of \$25,000. Negotiated indirect costs may be paid to the American University, Beirut, and the World Health Organization.

Indirect costs on training grants are limited to a fixed rate of eight percent of MTDC exclusive of tuition and related fees, direct expenditures for equipment, and sub-awards in excess of \$25,000.

If requesting indirect costs in the budget based on a federally negotiated rate, a copy of the indirect cost rate agreement is required. Include a copy of the current negotiated federal indirect cost rate agreement or cost allocation plan approval letter.

4. Review and Selection Process

Applications will be evaluated for scientific and technical merit by an appropriate peer review group, in accordance with CDC peer review policy and procedures, using the stated review criteria.

As part of the scientific peer review, all applications:

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

Applications will be assigned to the appropriate HHS/CDC Center, Institute, or Office. Applications will compete for available funds with all other recommended applications submitted in response to this NOFO. Following initial peer review, recommended applications will receive a second level of review. The following will be considered in making funding recommendations:

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

Additional consideration may be given for the following:

Component A and B:

- Number of potential participants in the recruitment pool for follow-up surveys
- Racial-ethnic diversity of potential participants in the recruitment pool for follow-up surveys

Component D:

- Provision of secure access to high-capacity computing servers that meets Federal standards for security and confidentiality for approved SEED investigators

Review of risk posed by applicants.

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

In accordance 41 U.S.C. 2313, CDC is required to review the non-public segment of the OMB-designated integrity and performance system accessible through SAM (currently the

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

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

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

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

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

5. Anticipated Announcement and Award Dates

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

Section VI. Award Administration Information

1. Award Notices

Any applications awarded in response to this NOFO will be subject to the DUNS, SAM Registration, and Transparency Act requirements. If the application is under consideration for funding, HHS/CDC will request "just-in-time" information from the applicant as described in the HHS Grants Policy Statement

(<https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf>).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the Grants Management Officer is the authorizing document and will be sent via email to the grantee's business official.

Recipient must comply with any funding restrictions as described in Section IV.11. Funding Restrictions. Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be allowable as an expanded authority, but only if authorized by CDC.

2. CDC Administrative Requirements

Overview of Terms and Conditions of Award and Requirements for Specific Types of Grants

Administrative and National Policy Requirements, Additional Requirements (ARs) outline the administrative requirements found in 45 CFR Part 75 and the HHS Grants Policy Statement and other requirements as mandated by statute or CDC policy. Recipients must comply with administrative and national policy requirements as appropriate. For more information on the Code of Federal Regulations, visit the National Archives and Records Administration:

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

Specific requirements that apply to this NOFO are the following:

[AR-1: Human Subjects Requirements](#)

[AR-2: 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 2030](#)

[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-21: Small, Minority, And Women-owned Business](#)

[AR-22: Research Integrity](#)

[AR-24: Health Insurance Portability and Accountability Act Requirements](#)

[AR-25: Data Management and Access – new requirement](#)

[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 Nonresearch

[AR-32: FY 2015 Enacted General Provisions](#)

[AR-4: HIV/AIDS Confidentiality Provisions](#)

AR-5: HIV Program Review Panel Requirements

AR-6: Patient Care

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

[AR-18: Cost Recovery – ATSDR](#)

[AR-19: Third Party Agreements – ATSDR](#)

[AR-20: Conference Support](#)

[AR-27: Conference Disclaimer and Use of Logos](#)

[AR-8: Public Health System Reporting Requirements](#)

AR-15: Proof of Non-profit Status

[AR-23: Compliance with 45 C.F.R. Part 87](#)

3. Additional Policy Requirements

The following are additional policy requirements relevant to this NOFO:

HHS Policy on Promoting Efficient Spending: Use of Appropriated Funds for Conferences and Meetings, Food, Promotional Items and Printing Publications This policy supports the Executive Order on Promoting Efficient Spending (EO 13589), the Executive Order on Delivering and Efficient, Effective, and Accountable Government (EO 13576) and the Office of Management and Budget Memorandum on Eliminating Excess Conference Spending and Promoting Efficiency in Government (M-35-11). This policy apply to all new obligations and all funds appropriated by Congress. For more information, visit the HHS website at: <https://www.hhs.gov/grants/contracts/contract-policies-regulations/efficient-spending/index.html>.

Federal Funding Accountability and Transparency Act of 2006 Federal Funding Accountability and Transparency Act of 2006 (FFATA), P.L. 109–282, as amended by section 6202 of P.L. 110–252, requires full disclosure of all entities and organizations receiving Federal

funds including grants, contracts, loans and other assistance and payments through a single, publicly accessible website, www.usaspending.gov. For the full text of the requirements, please review the following website: <https://www.fsr.gov/>.

Plain Writing Act The Plain Writing Act of 2010, Public Law 111-274 was signed into law on October 13, 2010. The law requires that federal agencies use "clear Government communication that the public can understand and use" and requires the federal government to write all new publications, forms, and publicly distributed documents in a "clear, concise, well-organized" manner. For more information on this law, go to: <http://www.plainlanguage.gov/plLaw/index.cfm>.

Pilot Program for Enhancement of Employee Whistleblower Protections All applicants will be subject to a term and condition that applies the terms of 48 CFR section 3.908 to the award and requires that grantees inform their employees in writing (in the predominant native language of the workforce) of employee whistleblower rights and protections under 41 U.S.C. 4712.

Copyright Interests Provision This provision is intended to ensure that the public has access to the results and accomplishments of public health activities funded by CDC. Pursuant to applicable grant regulations and CDC's Public Access Policy, Recipient agrees to submit into the National Institutes of Health (NIH) Manuscript Submission (NIHMS) system an electronic version of the final, peer-reviewed manuscript of any such work developed under this award upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. Also at the time of submission, Recipient and/or the Recipient's submitting author must specify the date the final manuscript will be publicly accessible through PubMed Central (PMC). Recipient and/or Recipient's submitting author must also post the manuscript through PMC within twelve (12) months of the publisher's official date of final publication; however the author is strongly encouraged to make the subject manuscript available as soon as possible. The recipient must obtain prior approval from the CDC for any exception to this provision.

The author's final, peer-reviewed manuscript is defined as the final version accepted for journal publication, and includes all modifications from the publishing peer review process, and all graphics and supplemental material associated with the article. Recipient and its submitting authors working under this award are responsible for ensuring that any publishing or copyright agreements concerning submitted articles reserve adequate right to fully comply with this provision and the license reserved by CDC. The manuscript will be hosted in both PMC and the CDC Stacks institutional repository system. In progress reports for this award, recipient must identify publications subject to the CDC Public Access Policy by using the applicable NIHMS identification number for up to three (3) months after the publication date and the PubMed Central identification number (PMCID) thereafter.

Language Access for Persons with Limited English Proficiency Recipients of federal financial assistance from HHS must administer their programs in compliance with federal civil rights law. This means that recipients of HHS funds must ensure equal access to their programs without regard to a person's race, color, national origin, disability, age and, in some circumstances, sex and religion. This includes ensuring your programs are accessible to persons

with limited English proficiency. Recipients of federal financial assistance must take the reasonable steps to provide meaningful access to their programs by persons with limited English proficiency.

Dual Use Research of Concern On September 24, 2014, the US Government Policy for the Institutional Oversight of Life Sciences Dual Use Research of Concern was released. Grantees (foreign and domestic) receiving CDC funding on or after September 24, 2015 are subject to this policy. Research funded by CDC involving the agents or toxins named in the policy, must be reviewed to determine if it involves one or more of the listed experimental effects and if so, whether it meets the definition of DURC. This review must be completed by an Institutional Review Entity (IRE) identified by the funded institution.

Recipients also must establish an Institutional Contact for Dual Use Research (ICDUR). The award recipient must maintain records of institutional DURC reviews and completed risk mitigation plans for the term of the research grant, cooperative agreement or contract plus three years after its completion, but no less than eight years, unless a shorter period is required by law or regulation.

If a project is determined to be DURC, a risk/benefit analysis must be completed. CDC will work collaboratively with the award recipient to develop a risk mitigation plan that the CDC must approve. The USG policy can be found at <http://www.phe.gov/s3/dualuse>.

Non-compliance with this Policy may result in suspension, limitation, restriction or termination of USG funding, or loss of future USG funding opportunities for the non-compliant USG-funded research project and of USG funds for other life sciences research at the institution, consistent with existing regulations and policies governing USG funded research, and may subject the institution to other potential penalties under applicable laws and regulations.

Data Management Plan(s)

CDC requires that all new collections of public health data include a Data Management Plan (DMP). For purposes of this announcement, “public health data” means digitally recorded factual material commonly accepted in the scientific community as a basis for public health findings, conclusions, and implementation.

This new requirement ensures that CDC is in compliance with the following; Office of Management and Budget (OMB) memorandum titled “Open Data Policy—Managing Information as an Asset” (OMB M-13-13); Executive Order 13642 titled “Making Open and Machine Readable the New Default for Government Information”; and the Office of Science and Technology Policy (OSTP) memorandum titled “Increasing Access to the Results of Federally Funded Scientific Research” (OSTP Memo).

The AR-25 <https://www.cdc.gov/grants/additional-requirements/ar-25.html> outlines the components of a DMP and provides additional information for investigators regarding the requirements for data accessibility, storage, and preservation.

Certificates of Confidentiality: Institutions and investigators are responsible for determining whether research they conduct is subject to Section 301(d) of the Public Health Service (PHS)

Act. Section 301(d), as amended by Section 1012 of the 21st Century Cures Act, P.L. 114-255 (42 U.S.C. 241(d)), states that the Secretary shall issue Certificates of Confidentiality (Certificates) to persons engaged in biomedical, behavioral, clinical, or other research activities in which identifiable, sensitive information is collected. In furtherance of this provision, CDC supported research commenced or ongoing after December 13, 2016 in which identifiable, sensitive information is collected, as defined by Section 301(d), is deemed issued a Certificate and therefore required to protect the privacy of individuals who are subjects of such research. Certificates issued in this manner will not be issued as a separate document, but are issued by application of this term and condition to this award. See Additional Requirement 36 to ensure compliance with this term and condition. The link to the full text is at: <https://www.cdc.gov/grants/additional-requirements/ar-36.html>.

4. Cooperative Agreement Terms and Conditions

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Part 75, and other DHHS, PHS and CDC regulations and 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 awardees 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 awardees for the project, although specific tasks and activities may be shared among the awardees and HHS/CDC as defined below.

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

- Oversight of project management and all scientific aspects of the project at their site and for the study overall in collaboration with other site PIs and the SEED Network Science Lead at CDC.
- Obtaining documentation and providing support for approval of any necessary differences from the single approved IRB protocol based on jurisdictional and/or institutional-specific requirements and adhering to CDC provisions of the Certificate of Confidentiality.
- Working collaboratively as members of the SEED Network with the CDC SEED Network Science Lead and other CDC scientists and administrators on aspects of protocol development, study implementation, data collection, and study conduct.
- Actively participating in SEED meetings, webinars, workgroup meetings, and conference calls. Ensure timely responses to all Quality Assurance/Quality Control (QA/QC) activities related to SEED.

- Adhering to the established SEED Publication and Data Sharing Guidelines. These guidelines include CDC-specific scientific requirements pertaining to CDC clearance and have been developed to meet Federal guidelines for data sharing.
- Using the CDC-approved mechanism for access to and use of SEED participant tracking and analytic files, which will ensure that all Federal standards for security and confidentiality are maintained.
- Implementing a standard SEED Data Management Plan established by CDC and a central interviewing contractor.

Awardees 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:

- Provide awardees a standard SEED Data Management Plan that will be implemented following award.
- Provide management oversight and scientific consultation as requested by the Awardees.
- Support the Awardees' activities by consulting and providing scientific and public health consultation and assistance in the development of activities related to the cooperative agreement.
- Assist in facilitating communication among the Awardees for the development of common multi-center protocol(s), quality control, interim data monitoring, data analyses, interpretation, reporting and coordination.
- Ensure adherence of human subject requirements and approval of single IRB study protocol.
- Collaborate to produce technical reports and manuscripts for peer-reviewed publications as appropriate. Aid with joint analysis with aggregate data.

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

Additionally, 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:

Components A and B:

The planning and implementation of the cooperative aspects of the study will be undertaken by the SEED site PIs and the SEED Network Science Lead at CDC. This group will work to

formulate plans for cooperative research and address issues of common concern throughout the life of the project. At periodic meetings among all awardees, the groups will

1. Develop the final protocol for the follow-up study assessment;
2. Discuss any difficulties in implementing the methodology for the study;
3. Identify how to reconcile differences in approaches to the study;
4. Identify and recommend solutions to unexpected study problems;
5. Discuss ways to efficiently coordinate study activities and best practices;
6. Work together in various workgroups and committees, including a PI Workgroup, the Data Sharing Committee, and the Derived Variable Workgroup to establish a library of investigator-derived variables;
7. Participate in calls with the survey contractor to discuss operations;
8. The SEED Data Sharing Committee will review and comment on requests to use the SEED dataset for research analyses and publications resulting from these analyses.

Component D:

The planning and implementation of an expert meeting to establish priorities for genetic analyses and use of SEED biospecimens, and the establishment of partnerships with ASD researchers with genetic expertise will be undertaken by the site PI and the SEED Network Science Lead at CDC with ongoing consultation from the SEED site PIs.

5. Reporting

Recipients will be required to complete Research Performance Progress Report (RPPR) in eRA Commons at least annually (see <https://grants.nih.gov/grants/rppr/index.htm>; https://grants.nih.gov/grants/forms/report_on_grant.htm) and financial statements as required in the HHS Grants Policy Statement.

A final progress report, invention statement, equipment inventory list and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the HHS Grants Policy Statement.

Although the financial plans of the HHS/CDC CIO(s) provide support for this program, awards pursuant to this funding opportunity depend upon the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports) and the determination that continued funding is in the best interest of the Federal government.

The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for recipients of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later.

Compliance with this law is primarily the responsibility of the Federal agency. However, two elements of the law require information to be collected and reported by recipients:

- 1) Information on executive compensation when not already reported through the SAM Registration; and
- 2) Similar information on all sub-awards/ subcontracts/ consortiums over \$25,000. It is a requirement for recipients of Federal grants to report information about first-tier subawards and

executive compensation under Federal assistance awards issued in FY2011 or later. All recipients of applicable CDC grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov on all subawards over \$25,000. See the HHS Grants Policy Statement (<https://www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf>).

A. Submission of Reports

The Recipient Organization must provide HHS/CDC with an original, plus one hard copy of the following reports:

1. **Yearly Non-Competing Grant Progress Report**, is due 90 to 120 days before the end of the current budget period. The RPPR form (<https://grants.nih.gov/grants/rppr/index.htm>; https://grants.nih.gov/grants/rppr/rppr_instruction_guide.pdf) is to be completed on the eRA Commons website. The progress report will serve as the non-competing continuation application. Although the financial plans of the HHS/CDC CIO(s) provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports) and the determination that continued funding is in the best interest of the Federal government.
2. **Annual Federal Financial Report (FFR) SF 425** (https://grants.nih.gov/grants/forms/report_on_grant/federal_financial_report_ffr.htm) is required and must be submitted through 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 should include:

- Description of Progress during Annual Budget Period: Current Budget Period Progress reported on the RPPR form in eRA Commons (<https://grants.nih.gov/grants/rppr/index.htm>). Detailed narrative report for the current budget period that directly addresses progress towards the Measures of Effectiveness included in the current budget period proposal.
- Research Aims: list each research aim/project

a) Research Aim/Project: purpose, status (met, ongoing, and unmet), challenges, successes, and lessons learned

b) Leadership/Partnership: list project collaborations and describe the role of external partners.

- Translation of Research (1 page maximum). When relevant to the goals of the research project, the PI should describe how the significant findings may be used to promote, enhance, or advance translation of the research into practice or may be used to inform public health policy. This section should be understandable to a variety of audiences, including policy makers, practitioners, public health programs, healthcare institutions, professional organizations, community groups, researchers, and other potential users. The PI should identify the research findings that were translated into public health policy or practice and how the findings have been or may be adopted in public health settings. Or, if they cannot be applied yet, this section should address which research findings may be translated, how these findings can guide future research or related activities, and recommendations for translation. If relevant, describe how the results of this project could be generalized to populations and communities outside of the study. Questions to consider in preparing this section include:
 - How will the scientific findings be translated into public health practice or inform public health policy?
 - How will the project improve or effect the translation of research findings into public health practice or inform policy?
 - How will the research findings help promote or accelerate the dissemination, implementation, or diffusion of improvements in public health programs or practices?
 - How will the findings advance or guide future research efforts or related activities?
- Public Health Relevance and Impact (1 page maximum). This section should address improvements in public health as measured by documented or anticipated outcomes from the project. The PI should consider how the findings of the project relate beyond the immediate study to improved practices, prevention or intervention techniques, inform policy, or use of technology in public health. Questions to consider in preparing this section include:
 - How will this project lead to improvements in public health?
 - How will the findings, results, or recommendations been used to influence practices, procedures, methodologies, etc.?
 - How will the findings, results, or recommendations contributed to documented or projected reductions in morbidity, mortality, injury, disability, or disease?
- Current Budget Period Financial Progress: Status of obligation of current budget period funds and an estimate of unobligated funds projected provided on an estimated FFR.
- New Budget Period Proposal:
 - Detailed operational plan for continuing activities in the upcoming budget period, including updated Measures of Effectiveness for evaluating progress during the upcoming budget period. Report listed by Research Aim/Project.
 - Project Timeline: Include planned milestones for the upcoming year (be specific and provide deadlines).

- **New Budget Period Budget:** Detailed line-item budget and budget justification for the new budget period. Use the CDC budget guideline format.
- **Publications/Presentations:** Include publications/presentations resulting from this CDC grant only during this budget period. If no publication or presentations have been made at this stage in the project, simply indicate "Not applicable: No publications or presentations have been made."
- **IRB Approval Certification:** Include all current IRB approvals to avoid a funding restriction on your award. If the research does not involve human subjects, then please state so. Please provide a copy of the most recent local IRB and CDC IRB, if applicable. If any approval is still pending at time of APR due date, indicate the status in your narrative.
- **Update of Data Management Plan:** The DMP is considered a living document that will require updates throughout the lifecycle of the project. Investigators should include any updates to the project's data collection such as changes to initial data collection plan, challenges with data collection, and recent data collected. Applicants should update their DMP to reflect progress or issues with planned data collection and submit as required for each reporting period.
- **Additional Reporting Requirements:**

N/A

2. Annual Federal Financial Reporting The Annual Federal Financial Report (FFR) SF 425 is required and must be submitted through eRA Commons within 90 days after the end of the calendar quarter in which the budget period ends. The FFR should only include those funds authorized and disbursed during the timeframe covered by the report. The final FFR must indicate the exact balance of unobligated funds and may not reflect any unliquidated obligations. There must be no discrepancies between the final FFR expenditure data and the Payment Management System's (PMS) cash transaction data.

Failure to submit the required information in a timely manner may adversely affect the future funding of this project. If the information cannot be provided by the due date, you are required to submit a letter explaining the reason and date by which the Grants Officer will receive the information.

The due date for final FFRs will continue to be 90 days after the Period of Performance end date.

Recipients must submit closeout reports in a timely manner. Unless the Grants Management Officer (GMO) of the awarding Institute or Center approves an extension, recipients must submit a final FFR, final progress report, and Final Invention Statement and Certification within 90 days of the end of grant period. Failure to submit timely and accurate final reports may affect future funding to the organization or awards under the direction of the same Project Director/Principal Investigator (PD/PI).

FFR (SF 425) instructions for CDC recipients are now available at https://grants.nih.gov/grants/forms/report_on_grant/federal_financial_report_ffr.htm. For further information, contact GrantsInfo@nih.gov. Additional resources concerning the eFSR/FFR system, including a User Guide and an on-line demonstration, can be found on the eRA Commons Support Page: <https://grants.nih.gov/support/index.html>

FFR Submission: The submission of FFRs to CDC will require organizations to register with eRA Commons (Commons) (<https://era.nih.gov/>). CDC recommends that this one time registration process be completed at least 2 weeks prior to the submittal date of a FFR submission.

Organizations may verify their current registration status by running the “List of Commons Registered Organizations” query found at: https://era.nih.gov/registration_accounts.cfm. Organizations not yet registered can go to <https://era.nih.gov/> for instructions. It generally takes several days to complete this registration process. This registration is independent of Grants.gov and may be done at any time.

The individual designated as the PI on the application must also be registered in the Commons. The PI must hold a PI account and be affiliated with the applicant organization. This registration must be done by an organizational official or their delegate who is already registered in the Commons. To register PIs in the Commons, refer to the eRA Commons User Guide found at: https://era.nih.gov/docs/Commons_UserGuide.pdf.

3. Final Reports: Final reports should provide sufficient detail for CDC to determine if the stated outcomes for the funded research have been achieved and if the research findings resulted in public health impact based on the investment. The grantee’s final report should include:

- **Research Aim/Project Overview:** The PI should describe the purpose and approach to the project, including the outcomes, methodology and related analyses. Include a discussion of the challenges, successes and lessons learned. Describe the collaborations/partnerships and the role of each external partner.
- **Translation of Research Findings:** The PI should describe how the findings will be translated and how they will be used to inform policy or promote, enhance or advance the impact on public health practice. This section should be understandable to a variety of audiences, including policy makers, practitioners, public health programs, health care institutions, professional organizations, community groups, researchers and other potential end users. The PI should also provide a discussion of any research findings that informed policy or practice during the course of the period of performance. If applicable, describe how the findings could be generalized and scaled to populations and communities outside of the funded project.
- **Public Health Relevance and Impact:** This section should address improvements in public health as measured by documented or anticipated outcomes from the project. The

PI should consider how the findings of the project related beyond the immediate study to improved practices, prevention or intervention techniques, or informed policy, technology or systems improvements in public health.

- **Publications; Presentations; Media Coverage:** Include information regarding all publications, presentations or media coverage resulting from this CDC funded activity. Please include any additional dissemination efforts that did or will result from the project.
- **Final Data Management Plan:** Applicants must include an updated final Data Management Plan that describes the data collected, the location of where the data is stored (example: a repository), accessibility restrictions (if applicable), and the plans for long term preservation of the data.

Section VII. Agency Contacts

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

Application Submission Contacts

Grants.gov Customer Support (Questions regarding Grants.gov registration and submission, downloading or navigating forms)

Contact Center Phone: 800-518-4726

Email: support@grants.gov

Hours: 24 hours a day, 7 days a week; closed on Federal holidays

eRA Commons Help Desk (Questions regarding eRA Commons registration, tracking application status, post submission issues, FFR submission)

Phone: 301-402-7469 or 866-504-9552 (Toll Free)

TTY: 301-451-5939

Email: commons@od.nih.gov

Hours: Monday - Friday, 7am - 8pm U.S. Eastern Time

Scientific/Research Contact(s)

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

Email all inquiries to:

ResearchNOFO@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: kva5@cdc.gov

Financial/Grants Management Contact(s)

Mary Pat Shanahan

Grants Management Specialist

Office of Financial Services

Grants Services

Telephone: (412) 386-4453

Email: mpu0@cdc.gov

Section VIII. Other Information

Other CDC Notices of Funding Opportunities can be found at www.grants.gov.

All awards are subject to the terms and conditions, cost principles, and other considerations described in the HHS Grants Policy Statement.

Authority and Regulations

Awards are made under the authorization of Sections of the Public Health Service Act as

amended and under the Code Federal Regulations.

Sections 301(a) [42 U.S.C. Section 241(a)] and 317C of the Public Health Service Act [42 U.S.C. Section 247b-4)], as amended. Further authorization is provided under Pub. Law No. 106-310, Public Health Service Act; Pub. Law No. 109-416, Combating Autism Act of 2006; Public Law No. 113-157, Autism CARES Act of 2014; and Public Law No. 116-60, Autism CARES Act of 2019.

APPENDIX A:

Table. SEED 1-3 Cohort Description				
<i>SEED Phase</i>	<i>State abbreviations with geographic locations included in SEED</i>	<i>Birth Year of SEED participants</i>	<i>Age in years, 2022</i>	<i>Estimated no. of eligible participants: total and by final study class (ASD, DD, POP)</i>
1	CA, CO, GA, MD, NC, PA	2003-2006	16-19	2313 (613, 883, 817)
2	CA, CO, GA, MD, NC, PA	2008-2012	10-14	2028 (651, 709, 668)
3	CO, GA, MD, NC, WI, MO	2014-2017	5-8	1624 (421, 590, 571)*

*Estimated number of participants for SEED 3 are preliminary as the study is ongoing.

APPENDIX B:

FRAMEWORK – SEED FOLLOW-UP SURVEYS (Component A)

FRAMEWORK – SEED FOLLOW-UP SURVEYS (Component A)								
FIRST FOLLOW-UP SURVEY OF PARENTS INITIATED IN Y2: 40 MIN								
Co-occurring conditions & symptoms <i>Survey of diagnosed conditions</i> <i>Standardized parent questionnaire</i>	DSM-5 measure of level of supports needed <i>Survey</i>	Services and educational supports <i>Survey</i>	Community supports and social participation <i>Survey</i>	Safety and suicide <i>Survey</i>	Bullying and discrimination <i>Survey</i>	Healthcare needs and utilization <i>Survey</i>	Family and financial impacts <i>Survey</i>	Independence and adaptive behaviors <i>Standardized parent questionnaire</i>
FIRST FOLLOW-UP SURVEY SUPPLEMENTS BASED ON DEVELOPMENTAL PERIOD INITIATED IN Y2: 20 MIN								
MIDDLE CHILDHOOD SUPPLEMENT (SEED 3 cohort)			ADOLESCENT SUPPLEMENT (SEED 2 cohort)			ADULT CHILD (SEED 1 cohort)		
Executive functioning <i>Standardized parent questionnaire</i> Autism symptoms <i>Standardized parent questionnaire</i>			Transition planning; expected exit from high school <i>Survey</i> Parent-reported expectations <i>Survey</i> Autism symptoms <i>Standardized parent questionnaire</i>			Employment <i>Survey</i> Housing/independent living <i>Survey</i> Post-secondary education <i>Survey</i>		
SECOND FOLLOW-UP SURVEY OF SEED 1 PARTICIPANTS – PARENTS INITIATED AFTER EXIT FROM HIGH SCHOOL AND ADULT CHILDREN								
PARENT COMPONENT (10 MIN)				ADULT CHILD COMPONENT (40 MIN)				
Changes in healthcare needs and utilization <i>Survey</i> Vocational training and occupational support <i>Survey</i> Description of daily activities and social participation <i>Survey</i> Transition from high school to post-secondary education <i>Survey</i>				Depression screen <i>Questionnaire</i> Substance abuse screen <i>Survey</i> Quality of life <i>Survey or questionnaire</i> Social camouflaging <i>Survey or questionnaire</i> Sexuality, gender identity, and relationships <i>Survey</i>				

Note: sample standardized instruments are: Behavior Assessment System for Children, 3rd edition (BASC) for co-occurring symptoms; Vineland Adaptive Behavior Scales, 3rd edition Short Form (VABS) for independence and adaptive behaviors; Behavior Rating Inventory of Executive Function (BRIEF) for executive functioning; Social Responsiveness Scale, 2nd edition (SRS-2) for autism symptoms; Beck's Depression Inventory or Patient Health Questionnaire (PHQ) for adolescent depression screen; and the Camouflaging Autistic Traits Questionnaire (CAT-Q) for social camouflaging.

FRAMEWORK
IN-PERSON ASSESSMENT (Component B)

CORE ELEMENTS IN-PERSON ASSESSMENT
Cognitive functioning (e.g., Stanford-Binet 5 th ed., 45-60 min) <i>In person standardized instrument</i>
Potential In-person Supplements
Tasks designed to assess episodic memory, language, executive function, and/or motor abilities <i>e.g., NIH Toolbox – Cognitive Battery Behavior, Dells-Kaplan Executive Function System (D-KEFS)</i> Parent or Self-reported executive function questionnaires <i>e.g., Behavior Rating Inventory of Executive Function (BRIEF)</i> Measures of symptomatology associated with emotional and behavioral disorders <i>e.g., Child & Adolescent Symptom Inventory (CASI), Beck Depression Inventory (Beck)</i>

APPENDIX C: Questions and Answers from Potential Applicants for DD-21-001

Q1. Component A: What is the minimum total number of participants required?

Response to Q1: The NOFO does not specify a minimum total number of participants.

Q2. Component A: Is there a desired number from certain phases of SEED 1, 2, 3?

Response to Q2: The NOFO does not specify a desired number of participants from each phase of SEED. Under Section IV, #5. PHS 398 Research Plan Component, Component A/Capacity and Approach, Recruitment Pool, the NOFO states, “Provide the estimated number of SEED participants from phase 1, 2, and/or 3 available for potential inclusion in a follow-up survey.”

Q3. Component A and B: Eligible participants are required to have completed a clinic visit and appropriate developmental evaluation(s). Does that mean DD children in SEED 3 (who did not have a clinic visit) are not eligible for follow-up? This detail is important for resource planning.

Response to Q3: For Component A participant eligibility criteria for inclusion in the follow-up surveys will be updated when the NOFO is re-issued. Former SEED participants are eligible if they received a final study classification of ASD, DD or POP and the mother or primary caregiver consented to future follow-up (NOFO Section I, #2. Approach, Requirements for Component A, item #11).

For Component B, participant eligibility requirements also will be updated when the NOFO is re-issued. Former SEED participants are eligible if they 1) received a final class of ASD or DD in SEED 1,2, or 3; 2) completed the clinic visit, including the Mullen Scales of Early Learning during SEED 1,2 or 3; and 3) completed the first follow-up survey in Component A (Section I, #2. Approach, introduction to requirements for Component B).

Q4. Component A: Clarify the roles and responsibilities of the sites versus the roles and responsibilities of the Central Interviewing Contractor, especially with respect to recruitment, survey administration, and follow-up?

Response to Q4: Roles and Responsibilities are summarized in NOFO Section I, #2. Approach, Requirements for Component A, items #9-12. The table below summarizes roles and responsibilities for the Central Interviewing Contractor (also called the Contractor, or Central Interviewing Contractor) and Component A Awardees.

Activity	Responsible party	
	CDC/Central Interviewing Contractor	Component A Awardee
Obtain IRB approval under the new Common Rule requiring a single IRB for cooperative research supported by a Federal agency	Responsible *	Awardee's role limited to establishing a reliance arrangement with CDC's Institutional Review Board, seeking permission to: · Share Personally Identifiable Information (PII) · Seek informed consent from adult children
Develop electronic systems for · Participant tracking · Survey data collection	Responsible	Awardee's role limited to pilot testing and providing feedback
Conduct initial tracing to updated participant contact information	Not responsible	Responsible
Mail introductory packets	Not responsible	Responsible
Re-trace individuals with returned invitation packets	Responsible	Awardee's role limited to informing contractor of returned invitation packets and providing additional demographic data that may assist with locating current contact information, so long as they obtain permission to share PII
Conduct enrollment telephone calls	Central Interviewing Contractor will perform this activity in full, if awardee obtains permission to share PII with CDC	Awardee's role limited to initial call for pre-consent, and only if awardee unable to share PII with CDC
Conduct telephone interviews	Responsible	Not responsible
Follow-up calls to encourage participation	Responsible	Not responsible
Distribute incentives	Responsible	Not responsible

Obtain informed consent from adult children from SEED 1	Responsible	Not responsible
Respond to inquiries	Responsible	
Bi-weekly meetings to discuss progress and troubleshoot problems with implementation and progress toward enrollment and completion goals	Responsible Contractor will organize	Responsible Awardee will participate

- *indicates party responsible for activity

Q4a. Who is responsible for enrollment rates and completion rates?

Response to Q4a: While the Central Interviewing Contractor will be responsible for data collection after pre-enrollment, a number of activities are outlined the NOFO that Component A awardees will be expected to complete to support the Central Interviewing Contractor in achieving target enrollment and completion rates (Section I, #2. Approach, Requirements for Component A, #2. Approach, Requirements for Component A, items #11-12):

- **Item #11c** awardees are expected to inform the Central Interviewing Contractor of returned invitation packets and provide any available information to support addition contact tracing.
- **Item #12a** awardees are expected to conduct telephone calls to contact the participant and obtain permission to share PII and send list of participants to the Central Interviewing Contractor on a weekly basis; OR provide a list of participants to the Central Interviewing Contractor on a weekly basis of participants who have been sent an invitation packet and those packets that have been returned.
- **Item #12b** awardees are expected to meet by phone or web with the Central Interviewing Contractor on a bi-weekly basis to discuss study progress and troubleshoot any problems with study implementation
- **Item #12c** awardees are expected to serve as a point of contact for enrolled participants and assist with participant retention throughout the implementation of the initial and second follow-up survey.

Q4b. Will the Central Interviewing Contractor do contact tracing after initial invitations are sent by the sites?

Response to Q4b: The NOFO states that Component A awardees will inform the Central Interviewing Contractor of any returned invitation packets and provide any additional information available to support the Central Interviewing Contractor in completing additional tracing (Section I, #2. Approach, Requirements for Component A, item #11c).

Q4c. Will Central Interviewing Contractor do follow-up calls to encourage survey return, participation in data collection, or clarify missing data?

Response to Q4c: Yes, follow-up calls to encourage completion will be the responsibility of the

Central Interviewing Contractor.

Q4d. Will Central Interviewing Contractor distribute/budget incentives or will the sites be responsible for incentives? If the latter, what is the per participant incentive cost?

Response to Q4d: Yes, the Central Interviewing Contractor will be responsible for incentives.

Q4e. Will the Central Interviewing Contractor obtain permission from the caregiver to recruit the adult child for direct data collection or does the site do that upon pre-enrollment? Who obtains the adult child's contact information and does the actual recruitment?

Response to Q4e: Yes, the Central Interviewing Contractor will obtain permission from the caregiver to contact their adult child, obtain contact information, and recruit the adult child. Awardees are expected to work collaboratively with CDC, the Central Interviewing Contractor, and other Component A awardees to develop the protocol for obtaining informed consent from the adult child (Section I, #2. Approach, Requirements for Component A, item #9b). Further, awardees are expected to meet by phone or web with the Central Interviewing Contractor on a bi-weekly basis to discuss study progress and troubleshoot any problems with study implementation (Section I, #2. Approach, Requirements for Component A, item #12b) and to serve as a point of contact for enrolled participants, assisting with participant retention throughout the implementation of the initial and second follow-up surveys (Section I, #2. Approach, Requirements for Component A, item #12c).

Q4f. Does the Central Interviewing Contractor pay the costs of printing mailed surveys and standardized questionnaires noted in Appendix B if they are collecting that data?

Response to Q4f: Awardees will be responsible for mailing initial invitation packets and thus will be responsible for all included materials (Section I, #2. Approach, Requirements for Component A, item #11b). The primary mode of data collection will be through computer-assisted telephone interviews (CATI), which will be built and implemented by the Central Interviewing Contractor (Section I, #2. Approach, Requirements for Component A).

Q4g. Will it be possible for each individual site to develop a (separate) memorandum of understanding with the Central Interviewing Contractor that would facilitate sharing of participant information?

Response to Q4g: Yes the Central Interviewing Contractor will be expected to work with each Component A awardee to obtain approval a Data Use Agreement (DUA) to enable secure transmission of personally identifiable information (PII) including, but not limited to, address information and telephone numbers.

Q5. Component A: Is a contact tracing / recruitment system provided or will that need to be developed/budgeted by site?

Response to Q5: Awardees are expected to work collaboratively with CDC and the Central Interviewing Contractor to develop a secure centralized system to enter and store participant contact information. Development of the network-wide tracking system will be the responsibility of the Central Interviewing Contractor, but awardees will be expected to participate in pilot testing and providing feedback on all data systems, manuals and guidance as requested (Section I, #2. Approach, Requirements for Component A, item #10).

Q6. Component A: Is there an expected timeline for completing recruitment for survey 1

and follow-up surveys? Can recruitment extend across all 5 years of the award?

Response to Q6: Component A awardees should be working with the Central Interviewing Contractor throughout the funding period on initial tracing, mailing invitation packets, and providing additional participant information for retracing. Although these activities may not begin until 11 months after the award, it is anticipated that tracing of contact information will continue through Y4 and that the Central Interviewing Contractor will conduct surveys throughout the award period (Section I, #2. Approach, Requirements for Component A, items #11-12).

Q7. Component A: How does this initiative affect the “second follow-up survey of SEED1 participants”? Some will be over 18 at the first year of data collection while others will not yet be. Are we supposed to get all of cohort 1 in the first year? What is the timeframe spacing between the 1st follow up and 2nd follow up or this cohort?

Response to Q7: Component A awardees are expected to assist the Central Interviewing Contractor in enrolling and maintaining contact with SEED 1 participants for the second follow-up surveys during Years 2-5 (Section I, #2. Approach, Requirements for Component A, item #12). Second surveys of the adult children who previously participated in SEED will necessarily be conducted after the first follow-up survey with the adult child’s parents/primary caregiver because it is the parent/primary caregiver who provided consent for follow-up studies. As indicated (Section I, #2. Approach, Requirements for Component A, item #9), protocols will be developed collaboratively with input from CDC and Component A awardees for obtaining consent after the children from this SEED cohort have reached adulthood. The NOFO does not specify a maximum age.

Q8. Component A: Referring to page 35 of the RFA: Would a PII sharing agreement always be required? Consents for SEED 2 and 3 explicitly indicate state the entities authorized to share data (naming the sites). Does having this in place meet the requirements of the 2nd criteria?

Response to Q8: While the SEED 2 and 3 consents provide authorization, they do not guarantee willingness of an entity to share. To ensure sharing of this necessary information, the NOFO the applicant must be (1) the original entity that collected SEED data OR (2) have an established agreement with the entity that collected contact information from SEED participants (i.e., former SEED awardees) so that they can reach the SEED participants for the follow-up studies as outlined in this NOFO (Section III, #3. Additional Information on Eligibility/Component A).

Q9. What will be the mechanism for obtaining analytic SEED 1-3 data and merged data for this initiative? Will analytic data come from the Central Interviewing Contractor, Data Coordinating Center, or CDC?

Response to Q9: The awardee is responsible for contributing site-specific data to a pooled dataset that is maintained by CDC and accessed through a CDC-approved mechanism (Section I, #2. Approach, Requirements for Component A, item #14). The mechanism for distribution of data will be discussed among CDC and Component A awardees in Year 1 of the funding cycle, but will need to be through a CDC-approved mechanism that meets Federal standards for security and confidentiality mechanism (Section I, #2. Approach, Requirements for Component A, item #14).

Q10. If SEED 1 families have already participated in the SEED Teen Pilot, will they be re-contacted to collect additional new data pre-high school graduation in addition to a data collection event post-transition? (see also the timing question above related to this)

Response to Q10: Awardees are expected to assist the Central Interviewing Contractor in enrolling and maintaining contact with SEED 1 participants for the first follow-up surveys (Section I, #2. Approach, Requirements for Component A, items #11-12). Criteria for excluding SEED 1 participants who previously participated in the SEED Teen Pilot from some or part of the first follow-up survey will be discussed among Component A awardees and CDC during Y1 of the funding cycle.

Q11. Please confirm that this is considered a “New” submission for all sites since it is not a continuation or resubmission - thus, items 1 and 4 in the insert below are not required components of the application?

“From the top of page 40 of the RFA, the Research Plan describes the following Aims:

- 1. Introduction to Application** (for Resubmission and Revision ONLY) - provide a clear description about the purpose of the proposed research and how it addresses the specific requirements of the NOFO.
- 2. Specific Aims** – state the problem the proposed research addresses and how it will result in public health impact and improvements in population health.
- 3. Research Strategy** – the research strategy should be organized under 3 headings: Significance, Innovation and Approach. Describe the proposed research plan, including staffing and time line.
- 4. Progress Report Publication List** (for Continuation ONLY)

Response to Q11: Yes, this is considered a “New” submission, as specified under Part 1. Overview Information, Notice of Funding Opportunity Type.

Q12. Component A: Please clarify how many LOIs must be submitted per year of award. Clarify number required in year 2, since NOFO is inconsistent: 4. Submit Proposals for Analysis of SEED Data. Awardees are expected to submit proposals and obtain approval from the SEED Data Sharing Committee for at least one LOI each year in Year 1-2 and two LOIs each year in Year 2-5.

Response to Q12: The NOFO will be corrected at the next amendment to remove the conflicting statement of requirements for Y2. Two LOIs will be required in Y2.

Q13. Component A: For the required number of LOIs, analyses, and manuscripts, do the numbers reflect leadership by the awardee? Or does participation as a collaborator without leadership count?

Response to Q13: Each Awardee is expected to submit analysis proposals (LOIs) and complete analyses and manuscripts as outline in the NOFO (Section I, #2. Approach, Requirements for Component A, items #4-6). Submissions by other Awardees of former SEED sites do not meet this requirement.

Q14. Component A: Does the application have to list and provide rationale for the specific topics that will be addressed by the required number of LOIs?

Response to Q14: No, the NOFO does not specify that the rationale must be provided for specific topics.

Q15. Component A: Will it be possible for SEED 3 sites to use unobligated SEED 3 funds for the SEED Follow-Up Studies?

Response to Q15: Unobligated SEED 3 funds may not be used for the new funding opportunity.

Q16. Has the Central Interviewing Contractor been identified? If not, will there be a separate NOFO for this?

Response to Q16: The central interview contractor has not yet been identified. It will be funded through a contract mechanism (not a cooperative agreement) therefore there will not be a separate NOFO.

Q17. A Data Management Plan (DMP) is mentioned in several sections. It is unclear whether a detailed DMP must be included with the application or whether this RFA is requiring an indication of a commitment to develop the DMP post-award in collaboration with CDC. There is language indicating each in separate parts of the NOFO.

Response to Q17: The NOFO requires a commitment to adopt a standard SEED Data Management Plan (Section I, #2. Approach, Requirements for Component A item #14; Section I, #2. Approach, Requirements for Component B #6; Section I, #2. Approach, Requirements for Component C, item #5; Section I, #2. Approach, Requirements for Component D, item #6; Section I, #2 Approach, Collaboration/Partnerships). The standard SEED Data Management Plan will be established by CDC and the Central Interviewing Contractor in accordance with Federal data sharing requirements. Applicants do not need to develop a Data Management Plan, as this will be provided to recipients following award (Section V., #3 Additional Review Considerations).

Q18. Component C, is there a requirement that autoantibody assay data be deposited in a database managed by CDC? Or will the awardee provide datasets to parties interested in analyzing the data?

Response to Q18: Yes, the Component C awardee must store, enter, and transmit results of specimen testing and relevant data in a standardized and secure manner with common data elements mutually agreed upon with CDC. This will become part of a pooled data set and will be maintained and overseen by CDC according to a standard SEED Data Management Plan that meets Federal data sharing requirements. This data will be accessed by awardees and previous SEED sites through a CDC-approved mechanism that meets Federal standards for security and confidentiality (Section I, #2. Approach, Requirements for Component C, item #5).

Q19. Component C: If a site is not PI of a Component A application, but collaborates with another site on Component A, are they eligible to submit a Component C application as PI?

Response to Q19: To be funded for Component C, applicants must apply and be funded for Component A (Executive Summary).

Q20. Component C: If a site is not PI of a Component A application, can they be co-PI on a Component C application with a site that is submitting a Component A application?

Response to Q20: The NOFO specifies that to be funded for Component C, applicants must apply and be funded for Component A. Any applicant who applies for Component A may submit a separate application for Component B, C, D, and/or E (see NOFO Executive Summary). The NOFO does not specify any limits on the number of Components that a given applicant can apply for.

Q21. Component B: Is recruitment for component B dependent on completion of Component A?

Response to Q21: Yes, the Central Interviewing Contractor will send to the awardee a list of participants who are interested in completing the in-person visit among those who completed the first follow-up survey (Section I, #2. Approach, Requirements for Component B, item #4).

Q22. Component B: Is the Central Interviewing Contractor or the site doing the recruiting for the in-person visit? If site, will a local tracking system be needed or will site have access to the tracking system used by the Contractor? Who is responsible for data entry? Will scoring software be required on the site budget in order to produce feedback letters or will the Contractor produce those after site transmits data to them for entry?

Response to Q22: The Central Interviewing Contractor will send to the awardee a list of participants who are interested in completing the in-person visit. The awardee will be responsible for scheduling participants and following-up of families who were scheduled but did not complete the visit for any reason. As such, awardees will need to maintain a local tracking and data entry system (Section I, #2. Approach, Requirements for Component B, item #3-4).

Awardees are also responsible for generating and providing participant feedback letters within one month of the in-person visit. As such, awardees will need to generate and insert scores, as well as print and mail the feedback letter (Section I, #2. Approach, Requirements for Component B, item #5).

Data entry for the pooled data set will be discussed among awardees in the first year of funding.

Q23. What is the upper limit for the annual budget for Component A for ~800 participants?

Response to Q23: The average award for Component A in Budget Year 1 is anticipated to be \$425,000. The average award is based on an eligible sample of 800 participants, with the funding adjusted up or down based on the number of participants. The ceiling is \$750,000, which assumes the awardee will collaborate with two or more former SEED sites to contact participants and have a minimum of 2,400 eligible participants in their sample pool (NOFO Executive Summary)

Q24. If we cannot PI a proposal for Component A due to budget constraints, can we co-PI a component C proposal with another site that is submitting a Component A proposal?

Response to Q24: The NOFO specifies to be funded for Component C, applicants must apply and be funded for Component A. Any applicant who applies for Component A may submit a separate application for Component B, C, D, and/or E (NOFO Executive Summary). The NOFO does not specify any limits on the number of Components that a given applicant can apply for.

Q25. Component A: The NOFO says “e.g., postdoctoral fellow” but does not require postdoctoral level - we had considered a master’s level graduate supervised by a doctoral

level statistician. Is that not acceptable?

Response to Q25: A post-doctoral fellow is provided as an example of who could potentially fill this staffing position. However, as stated in the NOFO, this is an example – the requirement is for a total of 100% FTE per year of a person with sufficient training and experience to support data coding and analysis, data documentation and manuscript preparation (NOFO Section IV, #5 PHS 398 Research Plan Component, Management and Staffing, item #3b).

Q26: Component D: What is involved in "analytic support"?

Response to Q26: Analytic support involves serving as co-authors and/or co-analysts on genetic proposal within the SEED network. As stated in the NOFO (Section I, #2. Approach, Requirements for Component D, #7) it is expected that the Component D awardee will maintain expertise on the latest analytic methods that can be shared with approved SEED investigators, and that the awardee will serve as the primary analyst or as a supporting co-author on two LOI submissions each year involving genetic or epigenetic data. Additionally, the NOFO states that the Component D awardee is expected to have experience in developing measures and providing analytic support for copy number variant (CNV), single nucleotide polymorphism (SNP) and polygenetic risk score (PRS) level analyses (NOFO Section IV Application and Submission Information, #5. PHS 398 Research Plan Component, Analytic Support for Component D, item #2).

Q27: Component A: Is there an age eligibility for the 1st and 2nd contact? Some SEED 3 will be young and SEED 1 will be out of high school at study start.

Response to Q27: All participants from the SEED 1,2, 3 cohorts will be eligible for the first follow-up study – the NOFO does not state any age requirements and the first follow up will be completed by the child's parent/primary caregiver regardless of the child's age at the time of follow-up.

The purpose of the second follow-up survey of the child's parent/primary caregiver is to assess changes in service access and utilization that may occur following high school exit (NOFO Section I. Funding Opportunity Description, #1. Background and Purpose, pg. 8). The NOFO does not stipulate that child must be 18 years or older for the parent/primary caregiver to be eligible for the second follow-up survey, but it is anticipated that virtually all SEED 1 children will be 18 years or older by 2023.

Lastly, given that the self-report measures proposed for the second follow-up survey will be completed by the adult child. As stated in the NOFO, awardees are expected to work collaboratively with CDC, the Central Interviewing Contractor, and other Component A awardees to develop the protocol for obtaining informed consent from the children who participated in SEED 1, once they are adults (Section I, #2. Approach, Requirements for Component A, items #8c and 9b).

Q28: Component B: Who does the data entry of the Comp B instruments? Is the awardee or contractor paying the incentive?

Response to Q28: The Component B awardee will be responsible for data entry and paying the incentive for Component B activities. As stated in the NOFO, Component B awardees are responsible for following-up of families who were scheduled but did not complete the clinic visit for any reason. As such, awardees will need to maintain a local tracking and data entry

system (Section I, #2. Approach, Requirements for Component B, item #3-4). Awardees are also responsible for generating and providing participant feedback letters within one month of the in-person visit. As such, awardees will need to generate and insert scores, as well as print and mail the feedback letter (Section I, #2. Approach, Requirements for Component B, item #5), and will need to provide the monetary incentive.

Q29: Component B: B Comp intro mentions the relationship between IQ and adaptive. Was an adaptive measure not included under activities intentionally?

Response to Q29: An adaptive measure was not intentionally excluded. The exact measure to be implemented will be decided collaboratively among CDC and Component B awardees in the first year of funding.

Q30: Will the SEED1-3 (and new SEEDPlus) data be downloadable for local analysis, or will there be a central computing location such as the RDA? This affects our computing and analytic capacity planning.

Response to Q30: The awardee is responsible for contributing site-specific data to a pooled dataset that is maintained by CDC and accessed through a CDC-approved mechanism (Section I, #2. Approach, Requirements for Component A, item #14). The mechanism for distribution of data will be discussed among CDC and Component A awardees in Year 1 of the funding cycle, but will need to be through a CDC-approved mechanism that meets Federal standards for security and confidentiality mechanism that is similar to the current RDA (remote data access) platform being used for SEED 1-3 (Section I, #2. Approach, Collaboration/Partnerships, Component A).

Q31: The NOFO states that the CDC funding to the Colorado site was made to “JFK Partners and This University of Colorado School of Medicine” - however, the funding was actually awarded to the Regents of the University of Colorado. The NOFO is inaccurate which is impacting our ability to respond to the requirements on page 35.

Response to Q31: The NOFO will be amended to reflect the corrected information.

Q32: Pre-application Webinar Slide 41, Submission Issues. Include ERA commons to help with ASSIST. Update contact information on slides.

Response to Q32: The phone numbers for the eRA Service Desk listed on slide 28 are the same as what LC Browning mentioned during the Q&A session of the pre-application webinar (866-504-9552 or 301-402-7469). On slide 44, the TIMS phone number and website (ogstims@cdc.gov) are already listed.

Q33: For component D, are the following secure data access measures on a high performance compute cluster considered acceptable: (1) encrypted secure shell login with 2-factor authentication, (2) controlled access to SEED files via an ACL protocol, (3) log of users accessing data and any “inappropriate” download of data, (d) encrypted data storage devices?

Response to Q33: The NOFO states that the Component D awardee is expected to provide access to high-capacity computing servers for approved SEED investigators (Section I, #2. Approach, Requirements for Component D, item #5; Section I, #2. Approach, Collaboration/Partnerships, Component A), and that these servers must Federal standards for security and protection of confidentiality (Section IV, #5 PHS 398 Research Plan Component,

Component D, Capacity and Approach). Security for the high-power computing cluster should meet the standards outlined by National Institute of Standards and Technology (www.nist.gov). If considering use of cloud computing services, it will need to meet standards for approval by the Federal Risk and Authorization Management Program (www.FedRamp.gov). Please review the security you have proposed against these standards for your application. A final determination of your proposed security will be made at time of award. Enhancements may be requested at that time.

Q34: Component A. With respect to re-tracing would that require than some kind of memorandum of understanding because if the site is required to do the initial contact and pre consent before sharing that information, how would they then share that information?

Response to Q34: The NOFO states that Component A awardees will inform the Central Interviewing Contractor of any returned invitation packets and provide any additional information available to support the Central Interviewing Contractor in completing additional tracing (Section I, #2. Approach, Requirements for Component A, item #11c). However, if the awardee is unable to share the necessary personally identifiable information (PII), the awardee would need to assume responsibility for the portion of this activity requiring this information.

Q35: Can unobligated funds from SEED 3 be carried over to year 1 of the new grant?

Response to Q35: No. This is a new award, not a continuation. Therefore, unobligated funds from SEED 3 cannot be carried over to year 1 of the new grant.

Q36: Can there be a no cost extension on SEED 3?

Response to Q36: CDC will address no cost extensions on an individual basis once we approach the end of the funding period for Year 5.