Centers for Disease Control and Prevention

NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL

Understanding Polydrug Use Risk and Protective Factors, Patterns, and Trajectories to Prevent Drug Overdose

RFA-CE-22-011

02/24/2022

Table of Contents

Overview

Participating Organization(s)

Centers for Disease Control and Prevention

Components of Participating Organizations

Components of Participating Organizations:

National Center for Injury Prevention and Control

Notice of Funding Opportunity (NOFO) Title

Understanding Polydrug Use Risk and Protective Factors, Patterns, and Trajectories to Prevent Drug Overdose

Activity Code

Applications in response to this Notice of Funding Opportunity (NOFO) will be funded using the R01 activity code for a research grant.

Notice of Funding Opportunity Type

New

Agency Notice of Funding Opportunity Number

RFA-CE-22-011

Assistance Listings Number(s)

93.136

Category of Funding Activity

HL - Health

NOFO Purpose

This funding would support up to five (5) recipients for 3 years at up to $350,000 per award per year to conduct research to improve our understanding of **risk and protective factors, patterns, and trajectories** related to polydrug use, with a focus on polydrug combinations most likely to result in nonfatal overdose or death, such as combinations including synthetic opioids.

Polydrug combinations of interest include the following,

- Co-use of multiple opioids, knowingly or unknowingly (i.e., due to unknown adulterants)
- Co-use of non-opioid drugs (particularly psychostimulants [e.g., methamphetamine], cocaine, and benzodiazepines) AND opioids, knowingly or unknowingly
- Co-use of other combinations of drugs that may result in drug overdose

Applicants shall focus on identifying risk and protective factors, AND patterns, AND trajectories of polydrug use for either 1) the general population OR 2) one or more of the following subpopulations of interest:

- Persons who have experienced acute or chronic pain and used prescription opioids to manage their pain
- Persons who use cannabis, either medically or non-medically

Applicants may also use prior research or preliminary data to justify an alternate subpopulation of interest, such as other groups which have been disproportionately affected by overdose (e.g., those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups).

The overall goal of this research is to better understand risk and protective factors for and patterns and trajectories of polydrug use in order to inform focused drug use and overdose prevention efforts.

Key Dates

Publication Date:

To receive notification of any changes to RFA-CE-22-011, return to the synopsis page of this announcement at www.grants.gov and click on the "Send Me Change Notification Emails" link. An email address is needed for this service.

Letter of Intent Due Date:

01/07/2022

Letters of Intent are requested by **January 7, 2022**. Although a letter of intent is not required, is not binding, and does not enter into the review of an application, the information that it contains assists NCIPC staff with planning for scientific and technical merit peer review.

Application Due Date:

02/24/2022

Applications are due February 24, 2022 at 5:00PM EST. Please carefully review and follow the instructions in *Section IV. Application and Submission Information 9. Submission Dates and Times* in order to ensure timely receipt of your application by February 24, 2022 at 5:00PM EST.

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.

Applicants will use a system or platform to submit their applications through Grants.gov and eRA Commons to CDC. ASSIST, an institutional system to system (S2S) solution, or Grants.gov Workspace are options. ASSIST is a commonly used platform because it provides a validation of all requirements prior to submission and prevents errors.

For more information on 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 http://grants.nih.gov/support/index.html.

- E-mail: commons@od.nih.gov
- Phone: 301-402-7469 or (toll-free) 1-866-504-9552.
  Hours: Monday - Friday, 7 a.m. to 8 p.m. Eastern Time, excluding Federal holidays.

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:
05/03/2022
This is an estimated date.

Secondary Review:
07/11/2022
This is an estimated date.

Estimated Start Date:
09/30/2022
September 30, 2022

Expiration Date:
03/31/2022

Required Application Instructions

It is critical that applicants follow the instructions in the How to Apply - 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 20 pages.

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

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

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

Executive Summary

Purpose:
This funding would support up to five (5) applications for 3 years at up to $350,000 per award per year to conduct research to improve our understanding of **risk and protective factors, patterns, and trajectories** related to polydrug use, with a focus on polydrug combinations most likely to result in nonfatal overdose or death, such as combinations including synthetic opioids.

Polydrug combinations of interest include the following,

- Co-use of multiple opioids, knowingly or unknowingly (i.e., due to unknown adulterants)
- Co-use of non-opioid drugs (particularly psychostimulants [e.g., methamphetamine], cocaine, and benzodiazepines) AND opioids, knowingly or unknowingly
- Co-use of other combinations of drugs that may result in drug overdose

Applicants shall focus on identifying risk and protective factors, AND patterns, AND trajectories of polydrug use for either 1) the general population OR 2) one or more of the following subpopulations of interest:

- Persons who have experienced acute or chronic pain and used prescription opioids to manage their pain
- Persons who use cannabis, either medically or non-medically

Applicants may also use prior research or preliminary data to justify an alternate subpopulation of interest, such as other groups which have been disproportionately affected by overdose (e.g., those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups, people with a history of substance use disorders and/or overdose).

The overall goal of this research is to better understand risk and protective factors for and patterns and trajectories of polydrug use in order to inform focused drug use and overdose prevention efforts.

Mechanism of Support: The funding mechanism for this Notice of Funding Opportunity (NOFO) will be a research grant (R-01).

Funds Available and Anticipated Number of Awards: NCIPC intends to commit approximately up to $1,750,000 (direct and indirect costs) in FY 2022 to fund up to five (5)

applications for this NOFO for a three-year project period. 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 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.

Budget and Project Period:
The maximum total funding for a single 12-month budget period is $350,000 (direct and indirect) per award.

Throughout the project period, CDC's commitment to continuation of awards will be conditional on the availability of funds, evidence of satisfactory progress by the recipient (as documented in required reports), scientific and technical merits of the competitive application to compete the research for the final three years, and the determination that continued funding is in the best interest of the Federal government.

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. Eligibility Information 1. Eligible Applicants* are eligible to apply.

Eligible Project Directors/Principal Investigators (PDs/PIs)
CDC does not make awards to individuals directly. 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. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply.

Applications in which the contact Eligible PD/PI meets NIH Early Stage Investigator (ESI) status, as verified via the NIH Determination of Investigator Status process, **and** whose application has a meritorious peer review score, may be considered for prioritization during the second level of review (see *Section V. Application Review Information 4. Review and Selection Process*). For the contact PD/PI Determination of Investigator Status:

- Prior to application submission, PD/PIs are encouraged to verify and/or enter the date of their terminal research degree or the end date of their post-graduate clinical training in their eRA Commons Profile to ensure the correct identification. NIH systems will automatically calculate the status of each investigator and display it within their eRA Commons personal profile. The ESI status of the PD/PIs on any R01 or R01 equivalent application will be flagged at time of submission. Investigators should make sure their status is correctly marked in their profile. If your status is incorrect, please contact the NIH eRA Service Desk.

Number of PDs/PIs
An application may name more than one PD/PI; their names must appear on the face page of the application. However:

- One (1) principal investigator must be designated as the contact PD/PI for all correspondence related to the application.
- All PD/PIs must include their eRA Commons Identification in the Credential Field of the Senior/Key Person Profile Component of the SF-424 (R&R) Application Package.
- Institutions/organizations proposing multiple PDs/PIs must visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF-424 (R&R) Application Guide.

Number of Applications
Eligible applicant organizations may submit more than one application to this NOFO, provided that each application is scientifically distinct. However, applicant institutions can submit only one application with the same contact PD/PI. Only one application per contact PD/PI will be funded under this announcement. If two or more applications from the same contact PD/PI are received for this NOFO, the only application that will be submitted for review will be the last application received based on the document's time and date stamp in Grants.gov (http://www.grants.gov). The applicant must ensure that duplicate applications are withdrawn prior to the application review date.

Additionally, applicant institutions submitting applications with essentially the same proposed research to two or more CDC/ATSDR NOFOs will not be funded under more than one NOFO.

Application Type. NEW

Special Date(s)
A pre-application teleconference call will not be conducted for this NOFO. Applicant questions to clarify information in the text of this NOFO during the NOFO open period are strongly encouraged. Please contact via email the Scientific/Research Contact, Peer Review Contact, or the Financial/Grants Management Contact listed in *Section VII. Agency Contacts* with questions. All applicant questions (personal or application related identifying information redacted) received by January 1, 2022 and NCIPC responses to these questions will be included in an amended NOFO that will be published approximately by **January 10, 2022**. Please see *Section VII. Agency Contacts* for specific contact information.

Application Materials. See *Section IV.1* for application materials.

Hearing Impaired. Telecommunications for the hearing impaired are available at: TTY: 1-888-232-6348.

Section I. Funding Opportunity Description

Statutory Authority

Awards are made under the authorization of Sections 301, 391(a)(2) and 392(a)(1) of the Public Health Service Act, as amended, (42 USC §§ 241, 280b(a)(2), and 280-0(a)(1).

1. Background and Purpose

Background

As the overdose epidemic in the United States continues to evolve and expand, there is increasing attention on the role of polydrug use in drug overdoses (Mattson et al., 2021; O'Donnell, Gladden, Mattson, Hunter & Davis, 2020). While most drug overdose deaths continue to involve opioids, a large and growing proportion also include other non-opioid drugs, which may be combined with opioids with or without the knowledge of the person using them (Ahmed, Rossen & Sutton, 2021; Mattson et al., 2021; Gladden, O'Donnell, Mattson & Seth, 2019; O'Donnell, Gladden, Mattson, Hunter & Davis, 2020; Drug Enforcement Agency [DEA], 2020). Polydrug combinations are also common and increasing in nonfatal overdoses (Hoots, Vivolo-Kantor & Seth, 2020; Liu, Scholl, Hoots & Seth, 2020). With polydrug use contributing to more overdoses each year, an improved understanding of the unique risk and protective factors for and patterns and trajectories of polydrug use is needed in order to address the evolving drug overdose epidemic. Better understanding patterns of drug use and trajectories leading to polydrug use and polydrug overdose can help inform focused drug use and overdose prevention efforts.

While polydrug use is not new, drug use treatment and overdose data suggest that patterns of polydrug use may be changing in ways that increase the risk of drug overdose. Drug treatment and overdose data suggest a decrease in the misuse of prescription opioids or use of heroin alone and an increase in the use of prescription opioids and heroin with synthetic opioids, such as illicitly manufactured fentanyl (Mattson et al, 2021; Gladden, O'Donnell, Mattson & Seth, 2019; Cicero, Ellis & Kasper, 2020; National Institute on Drug Abuse [NIDA], 2021). Overdose data also suggest increases in the co-use of synthetic opioids and stimulants, such as cocaine and methamphetamine, and an increase in the co-use of synthetic opioids and benzodiazepines (Kariisa et al, 2019; Hoots, Vivolo-Kantor & Seth, 2020; Cicero, Ellis & Kasper, 2020; NIDA, 2021).

The Drug Enforcement Agency continues to raise concern about the presence of synthetic opioids in the drug supply (DEA, 2020). Drug seizure data show small but increasing numbers of counterfeit pills containing synthetic opioids and stimulant samples mixed with synthetic opioids (DEA, 2020; Park et al, 2021). Such contamination of the drug supply may result in individuals using highly potent synthetic opioids (e.g., illicitly manufactured fentanyl) without their knowledge, increasing overdose risk. Others who use drugs may purposefully combine synthetic opioids with other opioids or non-opioids, which also has the potential to increase overdose risk. We need a better understanding of the patterns and trajectories leading to co-use of synthetic opioids and other drugs to better understand whether increases in opioids involved in overdose deaths are the result of intentional or unintentional use of both opioids and non-opioids and to inform overdose prevention strategies.

Risk factors for and patterns and trajectories of polydrug use and overdose may vary for different subpopulations, which in turn may benefit from different prevention approaches. Understanding differences in the risk factors for and patterns and trajectories of polydrug use in these subpopulations can help us to better target prevention efforts. Two subpopulations that are of

interest to the Division of Overdose Prevention (DOP) include persons who have experienced acute or chronic pain and used prescription opioids to manage their pain, and persons who use cannabis either medically or nonmedically. DOP is also interested in other subpopulations who have been disproportionately affected by drug overdose (e.g., persons experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups, people with a history of substance use disorders and/or overdose) and the specific risk factors for and patterns and trajectories of polydrug use among these subpopulations.

Opioid prescribing rates (CDC Prescribing website, Schieber et al., 2019) and rates of overdoses involving prescription opioids alone have fallen, with about 1 in 5 overdoses in 2019 involving a prescription opioid (Mattson et al., 2021). However, rates of overdose deaths involving prescription opioids combined with other synthetic opioids have been on an upward trend (Mattson et al., 2021). Individuals who overdose on prescription opioids may or may not have initially received an opioid prescription; however, it is critical to ensure that those who do receive opioid prescriptions to treat acute or chronic pain do not transition to polydrug use that would put them at increased risk of an overdose. Understanding risk and protective factors for the transition from use of prescription opioids for acute or chronic pain to misuse of prescription opioids combined with use of illicit opioids or use of other drugs is needed to identify prevention approaches.

While cannabis remains a Schedule I controlled substance federally, there is a recent trend toward state level legalization of cannabis. As of May 2021, 36 states and the District of Columbia (DC) had legalized comprehensive medical cannabis programs, and 17 states and DC had legalized adult, non-medical cannabis use (National Conference of State Legislatures [NCSL], 2021). While there is currently limited evidence of an association between cannabis use and changes in the rates and use patterns of other licit and illicit substances, there is moderate evidence that cannabis use increases the risk of developing substance dependence and/or substance use disorder for alcohol, tobacco, and other illicit drugs, especially if cannabis use initiation was earlier (during adolescence) and frequent (at least weekly) (National Academies of Science, Engineering, and Medicine [NASEM], 2017). As states continue to legalize cannabis, for either medical or non-medical use, it is important to understand whether cannabis use increases risk or potentially protects against overdose, as well as understand risk and protective factors for and, patterns and trajectories of polydrug use and overdose among people who use cannabis either medically or non-medically. In particular, understanding risk and protective factors and trajectories related to cannabis used to treat medical conditions versus non-medical use of cannabis and polysubstance use could help inform prevention and response strategies and communication strategies for increasing public awareness about the potential risks of cannabis, especially among populations at increased risk of experiencing adverse health and social effects associated with cannabis (e.g., youth and pregnant women).

The goal of this NOFO is for applications to propose research to improve our understanding of

risk factors, patterns, and trajectories of polydrug overdose. Understanding the risk factors for and trajectories of drug use leading to polydrug use—both among the general population and specific subpopulations—will help us to inform and target interventions to prevent polydrug use and polydrug overdose.

Involvement of communities, including state and/or local health departments, local governmental agencies and/or businesses, or community-based organizations is highly encouraged. The goals of this collaboration include ensuring the relevance of the research to the community and efficient and effective translation of research results for use by the community.

Purpose:
This funding would support up to five (5) applications for 3 years at up to $350,000 per award per year to conduct research to improve our understanding of **risk and protective factors, patterns, and trajectories** related to polydrug use, with a focus on polydrug combinations most likely to result in nonfatal overdose or death, such as combinations including synthetic opioids.

Polydrug combinations of interest include the following,

- Co-use of multiple opioids, knowingly or unknowingly (i.e., due to unknown adulterants)
- Co-use of non-opioid drugs (particularly psychostimulants [e.g., methamphetamine], cocaine, and benzodiazepines) AND opioids, knowingly or unknowingly
- Co-use of other combinations of drugs that may result in drug overdose

Applicants shall focus on identifying risk and protective factors, AND patterns, AND trajectories of polydrug use for either 1) the general population OR 2) one or more of the following subpopulations of interest:

- Persons who have experienced acute or chronic pain and used prescription opioids to manage their pain
- Persons who use cannabis, either medically or non-medically

Applicants may also use prior research or preliminary data to justify an alternate subpopulation of interest, such as other groups which have been disproportionately affected by overdose (e.g., those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups).

The overall goal of this research is to better understand risk and protective factors for and patterns and trajectories of polydrug use in order to inform focused drug use and overdose prevention efforts.

Considerations Regarding NOFO Scope:
RFA-CE-22-011 is intended to increase our understanding of the risk and protective factors,

AND patterns, AND trajectories of polydrug use for 1) the general population and/or 2) persons who have experienced acute or chronic pain and used prescription opioids to manage their pain, or persons who use cannabis, either medically or non-medically and/or other groups which have been disproportionately affected by overdose. **Applications proposing studies that do not address the risk and protective factors, AND patterns, AND trajectories of polydrug use will not be recommended for funding (see *Section V. Application Review Information, 4 Review and Selection Process*).**

For the purposes of this NOFO, the polydrug combinations of interest include the following,

- Co-use of multiple opioids, knowingly or unknowingly (i.e., due to unknown adulterants)
- Co-use of non-opioid drugs (particularly psychostimulants [e.g., methamphetamine], cocaine, and benzodiazepines) AND opioids, knowingly or unknowingly
- Co-use of other combinations of drugs that may result in drug overdose

While use of alcohol or tobacco may be considered in the analysis, co-use of drugs with alcohol or tobacco should not be a primary focus of the proposed research. **Applications proposing studies where the primary focus is on alcohol or tobacco will not be recommended for funding (see *Section V. Application Review Information, 4 Review and Selection Process*).**

Applications must focus on human subjects. **Applications proposing studies involving animal subjects will not be recommended for funding (see *Section V. Application Review Information, 4 Review and Selection Process*).**

Minority Serving Institutions: This NOFO seeks diversity among applicant institutions, research investigators, and partnering organizations to ensure researcher experience and research outcomes are applicable and beneficial to all segments of our population and social ecology. Applicants from or collaborating with Minority Serving Educational Institutions (MSIs) representative of and serving the community participating in the evaluation are highly encouraged. For the purpose of this NOFO, MSIs include Hispanic Serving Institutions (HSIs), Historically Black Colleges and Universities (HBCUs), Tribal Colleges and Universities (TCUs), and Alaska Native and Native Hawaiian Serving Institutions, as defined by the U.S. Department of Education. Meritorious applications from eligible MSIs or eligible institutions collaborating with MSIs, as evidenced by MSI inclusion in the SF-424 Senior/Key Personnel form, may be considered during the second level of review to broaden distribution of awards (see *Section V. Application Review Information 4. Review and Selection Process*).

Healthy People 2030 and other National Strategic Priorities

The overall goal of this research is to better understand risk and protective factors for and patterns and trajectories of polydrug use in order to inform focused drug use and overdose prevention efforts. These goals are aligned with the following Healthy People 2030 Objectives:

Injury Prevention
IVP-03: Reduce unintentional injury deaths
IVP-20: Reduce overdose deaths involving opioids
IVP-22: Reduce overdose deaths involving synthetic opioids other than methadone

Drug and Alcohol Use – General
SU-03: Reduce drug overdose deaths
SU-07: Reduce the proportion of adults who used drugs in the past month
SU-15: Reduce the proportion of people who had a drug use disorder in the past year
SU-17: Reduce the proportion of people who started using heroin in the past year
SU-20: Reduce the proportion of people who started misusing prescription opioids in the past year.

Public Health Impact
By the conclusion of this funding initiative, we will have an improved understanding of risk and protective factors, patterns, and trajectories associated with polydrug use and polydrug overdose, including the co-use of multiple opioids, the co-use of opioid and non-opioid drugs (specifically psychostimulants [e.g., methamphetamine], cocaine, and benzodiazepines). Depending on the focus of funded projects, we may also have an improved understanding of drug use trajectories among those who have experienced pain and used prescription opioids to manage their pain or among those who have used cannabis either medically or non-medically, or among other groups which have been disproportionately affected by overdose. This improved understanding will inform the development of focused drug use and overdose prevention efforts.

Relevant Work
This NOFO aligns with the vision, mission, and goals of the Division of Overdose Prevention. The vision of the Division of Overdose Prevention is to end drug overdose and related harms. The mission is to monitor, prevent, and reduce harms associated with drug use, misuse, and overdose. The goals of the Division of Overdose Prevention include reducing opioid overdose now, addressing emerging drug trends, and preventing drug use initiation or drug misuse among youth or young adults (details available at: Overdose Prevention Research Priorities (cdc.gov)).

This project addresses the following research priorities and questions:

1. Identifying risk and protective factors for drug overdose, with a focus on overdoses involving opioids, emerging drugs, and polydrug combinations.
    a. How do risk and protective factors and trajectories for use, misuse, substance use disorder, and overdose differ for prescription opioids, illicit opioids, and other emerging drug threats such as resurging methamphetamine and cocaine?
    b. What are risk and protective factors and trajectories related to polydrug use and overdose, including co-use of opioid and non-opioid drugs, with a focus on methamphetamine, cocaine, and benzodiazepines?
    c. How do these risk and protective factors and trajectories vary by sociodemographic and geographic characteristics at all levels of the social ecology?
2. Understanding of the unique risk and protective factors for the multiple trajectories related to medical and nonmedical adult cannabis use.

a. What are risk and protective factors and trajectories related to medical and nonmedical cannabis use, cannabis use disorder, and polysubstance use, especially among vulnerable populations?

Recent Division of Overdose Prevention Publications related to polydrug overdose:

- Gladden M, O'Donnell J, Mattson C, Seth P. Changes in Opioid-Involved Overdose Deaths by Opioid Type and Presence of Benzodiazepines, Cocaine, and Methamphetamine – 25 States, July-December 2017 to January-June 2018. MMWR Morb Mortal Wkly Rep 2019:68(34);737-744.
- Hoots B, Vivolo-Kantor A, Seth P. The rise in nonfatal and fatal overdoses involving stimulants with and without opioids in the United States. Addiction. Epub 2020, Jan 7. doi: 10.1111/add.14878
- Kariisa M, Scholl L, Wilson N, Seth P, Hoots B. Drug Overdose Deaths involving Cocaine and Psychostimulants with Abuse Potential – United States, 2003-2017. MMWR Morb Mortal Wkly Rep 2019:68(17);41-43.
- Liu S, Scholl L, Hoots B, Seth P. Nonfatal Drug and Polydrug Overdoses Treated in Emergency Departments — 29 States, 2018–2019. MMWR Morb Mortal Wkly Rep 2020;69(34);1149–1155.
- Mattson CL, Tanz LJ, Quinn K, Kariisa M, Patel P, Davis NL. Trends and Geographic Patterns in Drug and Synthetic Opioid Overdose Deaths — United States, 2013–2019. MMWR Morb Mortal Wkly Rep 2021;70:202–207.
- ODonnell J, Gladden RM, Mattson C, et al. Vital Signs: Characteristics of drug overdose deaths involving opioids and stimulants — 24 states and the District of Columbia, January–June 2019. MMWR Morb Mortal Wkly Rep 2020;69(35);1189–1197.

CDC currently funds 66 jurisdictions as part of its Overdose Data to Action Program (https://www.cdc.gov/drugoverdose/od2a/index.html), a non-research, programmatic cooperative agreement that began in September 2019. The program is focused on the complex and changing nature of the drug overdose epidemic, including polydrug use and overdose, and highlights the need for an interdisciplinary, comprehensive, and cohesive public health approach to preventing overdoses.

References:

1. Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2021. Designed by LM Rossen, A Lipphardt, FB Ahmad, JM Keralis, and Y Chong: National Center for Health Statistics. Available at https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
2. CDC. Prescribing practices. Available at https://www.cdc.gov/drugoverdose/data/prescribing/prescribing-practices.html
3. Cicero TJ, Ellis MS, Kasper ZA. Polysubstance use: a broader understanding of substance use during the opioid crisis. American journal of public health. 2020 Feb;110(2):244-50.
4. Drug Enforcement Administration. 2020 National Drug Threat Assessment.

5. Gladden RM, O'Donnell J, Mattson CL, Seth P. Changes in opioid-involved overdose deaths by opioid type and presence of benzodiazepines, cocaine, and methamphetamine—25 states, July–December 2017 to January–June 2018. Morbidity and Mortality Weekly Report. 2019 Aug 30;68(34):737.
6. Hoots B, Vivolo-Kantor A, Seth P. The rise in non-fatal and fatal overdoses involving stimulants with and without opioids in the United States. Addiction. 2020 May;115(5):946-58.
7. Kariisa M, Scholl L, Wilson N, Seth P, Hoots B. Drug overdose deaths involving cocaine and psychostimulants with abuse potential—United States, 2003–2017. Morbidity and mortality weekly report. 2019 May 3;68(17):388.
8. Liu S, Scholl L, Hoots B, Seth P. Nonfatal Drug and Polydrug Overdoses Treated in Emergency Departments—29 States, 2018–2019. Morbidity and Mortality Weekly Report. 2020 Aug 28;69(34):1149.
9. Mattson CL, Tanz LJ, Quinn K, Kariisa M, Patel P, Davis NL. Trends and geographic patterns in drug and synthetic opioid overdose deaths—United S/tates, 2013–2019. Morbidity and Mortality Weekly Report. 2021 Feb 12;70(6):202.
10. National Academies of Sciences, Engineering, and Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research.
11. National Conference of State Legislatures. State Medical Marijuana Laws. 2021. https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx
12. National Institute on Drug Abuse. Overdose death rates. 2021. Available at https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates
13. Park JN, Rashidi E, Foti K, Zoorob M, Sherman S, Alexander GC. Fentanyl and fentanyl analogs in the illicit stimulant supply: Results from US Drug seizure data, 2011–2016. Drug and alcohol dependence. 2021 Jan 1;218:108416.
14. O'Donnell J, Gladden RM, Mattson CL, Hunter CT, Davis NL. Vital signs: Characteristics of drug overdose deaths involving opioids and stimulants—24 states and the District of Columbia, January–June 2019. Morbidity and Mortality Weekly Report. 2020 Sep 4;69(35):1189.
15. Schieber LZ, Guy GP, Seth P, Young R, Mattson CL, Mikosz CA, Schieber RA. Trends and patterns of geographic variation in opioid prescribing practices by state, United States, 2006-2017. JAMA network open. 2019 Mar 1;2(3):e190665.

2. Approach

This NOFO is intended to support rigorous research studies to understand risk factors for and patterns and trajectories of polydrug use in order to inform efforts to prevent drug overdose. Researchers must demonstrate how findings can be used to inform efforts to prevent polydrug use and polydrug overdose. While use of alcohol or tobacco may be considered in the analysis, co-use of drugs with alcohol or tobacco should not be a primary focus of the proposed research. **Applications proposing studies where the primary focus is on alcohol or tobacco will not be recommended for funding (see *Section V. Application Review Information, 4 Review and Selection Process*).**

Rigorous research designs using quantitative or mixed methods that are appropriate to address the research questions are preferred. Primary data collection is encouraged.

The application should clearly describe the proposed research approach including 1) the theoretical or empirical evidence supporting the proposed strategy, 2) the data source(s) and data access plans, 3) the planned analyses and how the analytic approach is well suited to the data source, 4) the research scope, and 5) the proposed study design.

Research plans must describe the research question(s) of interest and the proposed hypothesis for the study, the proposed aims and objectives, and research study design to test the hypothesis, as well as the expected outcomes to be evaluated. The data sources, proposed analytic strategy, and the estimated sample size and power for analysis for outcomes of interest must be clearly specified.

Proposed data analysis plans must be appropriate for the research design, hypotheses, and data. Researchers must clearly demonstrate how they will anticipate and evaluate the effects of threats to the internal and external validity of the specified research design. Applicants must propose studies that can feasibly be completed within the requested budget and project period.

Objectives/Outcomes

Applicants are expected to focus on **all** three of the following primary research objectives:

1. Identify risk and protective factors for polydrug use; **AND**
2. Identify patterns of polydrug use. Patterns of drug use refers to descriptions of the drug use such as the combinations of drugs taken, the timing and sequence of such combinations (e.g., concurrent vs. simultaneous use), the route of administration, and whether co-use is intentional or unintentional (i.e., due to unknown adulterants); **AND**
3. Identify trajectories of polydrug use and overdose. An individual's drug use trajectory refers to an individual's subsequent drug use over time after initiation of a drug or other precipitating factor.

Applicants must propose research that examines all 3 of these primary objectives. These objectives are interrelated, so applicants do not necessarily need to propose separate analyses to address these outcomes; however, the proposed research and the planned outcomes must speak to all 3 of these objectives. The analytic methods should clearly describe how each objective will be met.

The goal of this research is to inform overdose prevention, so focus of this research must be on polydrug combinations and identifying trajectories toward polydrug use that are most likely to result in overdose (e.g., combining another drug with a synthetic opioid, such as illicitly manufactured fentanyl). Specific drug combinations of interest include co-use of opioids, co-use of opioids and non-opioid drugs (especially psychostimulants (e.g., methamphetamine), cocaine, and benzodiazepines).

Applicants may choose to focus on polydrug combinations in the general population; alternatively, applicants may choose to focus on one of the subpopulations of interest:

- Those who have experienced acute or chronic pain and used prescription opioids to manage their pain
- Those who use cannabis, either medically or non-medically

Alternatively, applicants may use prior research or preliminary data to justify an alternate subpopulation of interest, such as other groups which have been disproportionately affected by overdose (e.g., those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups, people with a history of substance use disorders and/or overdose).

Applicants who chose to focus on a subpopulation of interest must also focus on all 3 primary objectives (risk and protective factors for, patterns of, and trajectories of polydrug use) and combinations of drugs that are most likely to result in overdose, such as combinations including synthetic opioids.

While use of alcohol or tobacco may be considered in the analysis, co-use of drugs with alcohol or tobacco SHOULD NOT be a primary focus of the proposed research (e.g., co-use of alcohol and heroin is not considered poly*drug* use for the purpose of this NOFO).

Data collection, acquisition, and analysis.
Applicants must identify and describe appropriate data sources and provide evidence of their ability to acquire and/or collect data of sufficient quantity and quality to conduct the proposed research. Applications should clearly describe and justify the proposed sampling methods, sample size, power estimates, and data collection methods for each research objective. Appropriate data sources will vary by the approach selected, research goals, and the study design. Each objective should be measured at the level that best addresses the research question, the population of interest, and the data sources available or collected for the purposes of this project

Protection of Human Subjects and Personal Identifiable Information
The Research Strategy section of the application is expected to clearly describe the type, source, access to, and protections of the data and human subjects participating in the study. Access to non-publicly available, previously collected data must be clearly described in the Research Strategy and documented with a signed Data Sharing Agreement or Letter of Support. Access to publicly available, previously collected data must be clearly described in the Research Strategy.

Protection of previously collected data includes, but is not limited to, protection of personal identifiable information from loss and/or misuse.

The application is expected to identify each performance site that will be conducting human subjects research and include the FWA number for the applicant institution and each performance site. Research conducted with more than one institution will be expected to use a

single Institutional Review Board (sIRB) to conduct the ethical review required by HHS regulations. See ***Section IV. Application and Submission Information, 10 Funding Restrictions, Human Subjects*** for details.

Target Population

This research focuses on persons who co-use drugs illicitly or who may be at risk of illicit polydrug use, including the co-use of multiple opioids and co-use of opioid and non-opioid drugs (specifically psychostimulants [e.g., methamphetamine], cocaine, and benzodiazepines). Other target subpopulations include those who have experienced pain and used prescription opioids or those who use cannabis either medically or non-medically or other groups which have been disproportionately affected by overdose (e.g., those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups, people with a history of substance use disorders and/or overdose).

Collaboration/Partnerships

It is expected that for all applications, the applicant organization and contact PI will provide the scientific and technical leadership necessary to conduct the proposed research throughout the entire project period. It is expected that the proposed research work plan described in the Research Strategy section of the application and the SF-424 Research and Related Budget will demonstrate the applicant organization's leadership and involvement throughout the entirety of the project period. The applicant organization cannot serve as a "pass through" to fund another entity to conduct the majority of the research or provide the scientific or technical leadership necessary to complete the proposed research project.

As stated in the Background of this NOFO, NCIPC recognizes the importance of community conditions and community involvement in research to ensure the relevance of the research to the community and efficient and effective translation of research results for use by the community. Applicants are encouraged to seek and include the meaningful involvement of communities, including state and/or local health departments, local governmental agencies and/or businesses, and community-based organizations in the development and conduct of the proposed research, and in the translation and dissemination of research results.

As described below, each partnership between the applicant institution and outside entities must be clearly described in the Research Strategy section of the application and clearly documented with a signed Letter of Support (LOS), Memorandum of Understanding (MOU) or Data Sharing Agreement. Applications without documentation of each partnership may not be recommended for funding.

The Research Strategy section of the application is expected to clearly describe the roles and responsibilities of each research team member individually and each participating entity. The Research Strategy must describe how the partnership will allow the applicant to complete the proposed work and demonstrate the likely success of the partnership to accomplish the research goals. This includes partnerships that will provide or facilitate access to relevant outcome data,

or access to study populations. The Research Strategy section of the application must clearly describe the nature and extent of the proposed partnership, including the roles and responsibilities of the Principal Investigator(s) and of the outside entities or partner agencies, the existing working relationship, plans for the proposed research, the nature and extent of the involvement to be provided by the applicant institution and outside entity, the outside entity's scope of work, and how the partnership will ensure project success.

The roles and responsibilities described for each partnering entity must be substantiated with a signed Data Sharing Agreement, Letter or Support (LOS), or Memorandum of Understanding (MOU), and be included in the Letter of Support section of the application. The Data Sharing Agreement, Letter of Support (LOS), or Memorandum of Understanding (MOU) must describe the partner's commitment of resources, time, and personnel to the proposed research. **Applications that do not include a signed Data Sharing Agreement, Letter of Support, or Memorandum of Understanding from each partnering entity may not be recommended for funding (for details see *Section V. Application Review Information, 4 Review and Selection Process*).**

The Research Strategy section of the application must also describe all of the proposed data sources and processes used to assure data access for all proposed analyses to be completed within the project period. **Evidence of access to each proposed dataset described in the Research Strategy must be documented by a signed Data Sharing Agreement, Memoranda of Understanding, or Letter of Support detailing the data availability and describing each partner's commitment of resources, time, and personnel to the proposed research.** The proposed budget should include travel funding for research staff to directly meet with and monitor study implementation within both the program and partner sites if the sites are not local to the research investigators. **Applications that do not include a signed Data Sharing Agreement, Letter of Support, or Memorandum of Understanding from each partnering entity and source of data described in the Research Strategy section of the application may not be recommended for funding (**for details **see *Section V. Application Review Information, 4 Review and Selection Process*).**

Applications will be evaluated during peer review on:

- The extent to which the Research Strategy section clearly describes the roles and responsibilities of each partner involved in the proposed study.
- The extent to which the Research Strategy clearly describes the working relationships between the applicant institution and all partner organizations.
- The extent to which the Research Strategy clearly describes the involvement and scope of work each partner is willing to complete to ensure the success of the proposed research within the proposed project period.
- The extent to which the relationships and activities of the partnerships described in the Research Strategy, are documented by a signed Data Sharing Agreement, Letter of Support, or Memorandum of Understanding that clearly delineates the intent and capabilities of each partnership.

Minority Serving Institutions: This NOFO seeks diversity among applicant institutions,

research investigators, and partnering organizations to ensure researcher experience and research outcomes are applicable and beneficial to all segments of our population and social ecology. Applicants from or collaborating with Minority Serving Educational Institutions (MSIs) representative of and serving the community participating in the evaluation are highly encouraged. For the purpose of this NOFO, MSIs include Hispanic Serving Institutions (HSIs), Historically Black Colleges and Universities (HBCUs), Tribal Colleges and Universities (TCUs), and Alaska Native and Native Hawaiian Serving Institutions, as defined by the U.S. Department of Education. Meritorious applications from eligible MSIs or eligible institutions collaborating with MSIs, as evidenced by MSI inclusion in the SF-424 Senior/Key Personnel form, may be considered during the second level of review to broaden distribution of awards (see *Section V. Application Review Information 4. Review and Selection Process*).

This NOFO encourages the inclusion of early-stage investigators as members of the SF-424 Senior/Key Personnel research team to help build experience and expertise in overdose prevention research.

Applications should demonstrate that the research staff have the necessary skills and experience to ensure quality and timeliness of proposed activities. The participation of students and other researchers-in-training is encouraged. Applicants planning to incorporate training and/or mentorship roles into their research activities should describe the plans for the recruitment, training, and supervision of trainees/mentees and the ongoing quality assurance of their scientific products.

Evaluation/Performance Measurement

Applicants must evaluate and document performance during each stage of the research process, including partner development (if applicable), study development, recruitment and data collection, data management, data analysis, and data dissemination. The application is expected to include a clear description of relevant performance measures for each stage of the research project. Comparison of actual progress to the performance measures is expected to document whether research is progressing appropriately and in a timely manner, and whether the research activities are of high scientific quality.

Evaluation of the proposed project, that is, the degree to which a funded project is meeting its performance goals will be aided by a detailed project workplan and timeline, accompanied by discussion of how unanticipated delays or adverse events of any kind will be handled.

Translation Plan

Investigators are expected to develop a translation plan for the research findings. The plan should describe how the results will be disseminated to achieve the greatest impact. The translation plan should describe the subsequent activities necessary to move successful research results to the next phase of research or action. In particular, the plan should describe how the results can be used to inform focused drug use and overdose prevention efforts.

The application is expected to clearly describe the potential for widespread dissemination of the proposed research. Research findings should be disseminated through publications, including

articles in peer reviewed scientific journals, and "Research Briefs" for diverse audiences, as well as presentations at professional conferences, and in institutional and community-based venues.

The overall goal of this research is to better understand risk and protective factors for and patterns and trajectories of polydrug use in order to inform focused drug use and overdose prevention efforts. 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 description 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 could be translated into public health policy or practice and how the findings may be adopted in public health settings. Or, if they cannot be applied yet, this description should address which research findings may be translated, how these findings can guide future research or related activities, and recommendations for translation. In addition, the PI should describe how the findings may be used to address key drivers of health inequities, e.g., through focusing on disproportionately affected populations. Disproportionately affected populations may include persons experiencing a disproportionate burden of drug use and overdose, including but not limited, to those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups. If relevant, describe how the results of this project could be generalized to populations and communities outside of the study.

Applicants should also include plans to appropriately document the research methods as well as lessons learned to facilitate future replication. These plans may include but are not limited to documenting the methods and documenting lessons learned from the study that might inform decisions about future adaptation or modification of the approach for other settings or populations.

Grant recipients will be required to attend at least one reverse site visit in Atlanta with CDC/NCIPC staff during the duration of performance to review their progress and findings and to discuss opportunities for widespread dissemination of their research achievements and lessons learned. This must be reflected in the grantee's budget in their application submitted in response to this NOFO.

3. Funding Strategy

N/A

Section II. Award Information

Funding Instrument Type:
G (Grant)

A support mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity.

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:
$5,250,000
The maximum award amount will be $350,000 (direct and indirect costs) per award for the first 12-month budget period. This includes both direct and indirect costs. An applicant may request a project period of up to three years. The maximum total project funding amount is $1,050,000 (including both direct and indirect costs) per award over the expected 3-yr project period length. The maximum total funding over the three (3) year project period for up to five (5) awards is up to $5,250,000. The project period for each award is expected to run from 9/30/2022 to 9/29/2025.

Anticipated Number of Awards:
5
The anticipated number of awards that will be made under this NOFO is up to five (5) awards.

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

Award Ceiling:
$350,000
Per Budget Period

Award Floor:
$0
Per Budget Period

Total Period of Performance Length:
3 year(s)

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

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

If you are successful and receive a Notice of Award, in accepting the award, you agree that the award and any activities thereunder are subject to all provisions of 45 CFR Part 75, currently in effect or implemented during the period of the award, other Department regulations and policies in effect at the time of the award, and applicable statutory provisions.

Section III. Eligibility Information

1. Eligible Applicants

Eligibility Category:
00 (State governments)

01 (County governments)

02 (City or township governments)

04 (Special district governments)

05 (Independent school districts)

06 (Public and State controlled institutions of higher education)

07 (Native American tribal governments (Federally recognized))

08 (Public housing authorities/Indian housing authorities)

12 (Nonprofits having a 501(c)(3) status with the IRS, other than institutions of higher education)

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

13 (Nonprofits without 501(c)(3) status with the IRS, other than institutions of higher education)

20 (Private institutions of higher education)

22 (For profit organizations other than small businesses)

23 (Small businesses)

25 (Others (see text field entitled "Additional Information on Eligibility" for clarification))

99 (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:

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

Hispanic-serving Institutions

Historically Black Colleges and Universities (HBCUs)

Tribally Controlled Colleges and Universities (TCCUs)

Alaska Native and Native Hawaiian Serving Institutions

Nonprofits (Other than Institutions of Higher Education):

Nonprofits (Other than Institutions of Higher Education)

Other:

Faith-based or Community-based Organizations

Regional Organizations

Bona Fide Agents: A Bona Fide Agent is an agency/organization identified by the state as eligible to submit an application under the state eligibility in lieu of a state application. If applying as a bona fide agent of a state or local government, a legal, binding agreement from the state or local government as documentation of the status is required. Attach with "Other Attachment Forms."

Federally Funded Research and Development Centers (FFRDCs): FFRDCs are operated, managed, and/or administered by a university or consortium of universities, other not-for-profit or nonprofit organization, or an industrial firm, as an autonomous organization or as an identifiable separate operating unit of a parent organization. A FFRDC meets some special long-term research or development need which cannot be met as effectively by an agency's existing in-house or contractor resources. FFRDC's enable agencies to use private sector resources to accomplish tasks that are integral to the mission and operation of the sponsoring agency. For more information on FFRDCs, go to https://gov.ecfr.io/cgi-bin/searchECFR.

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

See *Section III. Eligibility Information*

4. Justification for Less than Maximum Competition

Not Applicable

5. Responsiveness

It is the applicant's responsibility to ensure that the application meets all responsiveness criteria listed in this section. Applications that do not meet all of the following responsiveness criteria will be considered nonresponsive and will not be forwarded for peer review.

- There must be an overall match between the proposed research objectives as described in the Specific Aims section of the application and the research objectives described in the Background and Purpose, Approach, and Objectives and Outcomes sections of this funding announcement. This NOFO seeks research to improve our understanding of **risk and protective factors, patterns, and trajectories** related to polydrug use, with a focus on polydrug combinations most likely to result in nonfatal overdose or death, such as combinations including synthetic opioids.

• The first paragraph of the Specific Aims section of the application must clearly describe the primary goals and objectives of the proposed research. **Applications that do not clearly propose research on risk and protective factors, patterns, and trajectories related to polydrug use in the Specific Aims section of the application will be considered non-responsive and will not be forwarded for peer review.**

- The SF-424 Biographical Sketch for the PI or Co-Investigator must include documentation of expertise in the area of drug use or overdose. The knowledge, experience, and expertise necessary to conduct this research and achieve proposed objectives must be documented with at least one first-authored, peer-reviewed publication as defined by the NIH National Library of Medicine in the relevant area of drug use or overdose, or by serving as a principal investigator on a research grant in drug use or overdose research. The citation of the relevant publication(s) or research experience must be clearly identified (by bold text or highlight) in the appropriate SF 424 Biographical Sketch. **Applications that do not include documentation to meet this requirement will be considered non-responsive and will not be forwarded for peer review.**

6. Required Registrations

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

PLEASE NOTE: For applications due on or after April 4, 2022, applicants must have a unique entity identifier (UEI) at the time of application submission. In preparation for the federal government's April 4, 2022, transition from the Data Universal Numbering System (DUNS) to the Unique Entity Identifier (UEI), applicants must obtain a UEI. The UEI is generated as part of SAM.gov registration. Current SAM.gov registrants have already been assigned their UEI and can view it in SAM.gov and grants.gov. Additional information is available on the GSA website, SAM.gov, and Grants.gov-Finding the UEI.

- (Foreign entities only): Special Instructions for acquiring a Commercial and Governmental Entity (NCAGE) Code: https://eportal.nspa.nato.int/AC135Public/Docs/US Instructions for NSPA NCAGE.pdf
- System for Award Management (SAM) – must maintain current registration in SAM (the replacement system for the Central Contractor Registration) to be renewed annually, SAM.gov.
- Grants.gov
- eRA Commons

All applicant organizations must register with Grants.gov. Please visit www.Grants.gov at least 30 days prior to submitting your application to familiarize yourself with the registration and

submission processes. The one-time registration process will take three to five days to complete. However, it is best to start the registration process at least two weeks prior to application submission.

All Senior/Key Personnel (including Program Directors/Principal Investigators (PD/PIs) must also work with their institutional officials to register with the eRA Commons or ensure their existing Principal 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 an 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.

PLEASE NOTE: For applications due on or after April 4, 2022, applicants must have a unique entity identifier (UEI) at the time of application submission. In preparation for the federal government's April 4, 2022, transition from the Data Universal Numbering System (DUNS) to the Unique Entity Identifier (UEI), applicants must obtain a UEI. The UEI is generated as part of SAM.gov registration. Current SAM.gov registrants have already been assigned their UEI and can view it in SAM.gov and grants.gov. Additional information is available on the GSA website, SAM.gov, and Grants.gov-Finding the UEI.

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 SAM.gov and the SAM.gov Knowledge Base.

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 NOFO 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.

Eligible applicant organizations may submit more than one application to this NOFO, provided that each application is scientifically distinct. However, applicant institutions can submit only one application with the same contact PD/PI. Only one application per contact PD/PI will be funded under this announcement. If two or more applications from the same contact PD/PI are received for this NOFO, the only application that will be submitted for review will be the last application received based on the document's time and date stamp in Grants.gov (http://www.grants.gov). The applicant must ensure that duplicate applications are withdrawn prior to the application review date.

Additionally, applicant institutions submitting applications with essentially the same proposed research to two or more CDC/ATSDR NOFOs will not be funded under more than one NOFO.

Section IV. Application and Submission Information

1. Address to Request Application Package

Applicants will use a system or platform to submit their applications through Grants.gov and eRA Commons to CDC. ASSIST, an institutional system to system (S2S) solution, or Grants.gov Workspace are options. ASSIST is a commonly used platform because, unlike other platforms, it provides a validation of all requirements prior to submission and prevents errors.

To use ASSIST, applicants must visit https://public.era.nih.gov 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: http://grants.nih.gov/support/index.html

- Email: commons@od.nih.gov
- Phone: 301-402-7469 or (toll-free) 1-866-504-9552.
  Hours: Monday - Friday, 7 a.m. to 8 p.m. Eastern Time, excluding Federal holidays.

2. Content and Form of Application Submission

Applicants must use FORMS-G application packages for due dates on or after April 4, 2022 and must use FORMS-F application packages until April 3, 2022.

Application guides for FORMS-F and FORMS-G application packages are posted to the How to Apply - Application Guide page.

It is critical that applicants follow the instructions in the SF-424 (R&R) Application Guide How to Apply - Application Guide 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.

Please use the form and instructions for SF424 (R&R) Form F. Applicants must use FORMS-F application packages until April 3, 2022.

3. Letter of Intent

Due Date for Letter Of Intent 01/07/2022

01/07/2022

The requested due date for the Letter of Intent is **Janaury 7, 2022**. Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NCIPC 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 (organization)
- Description of the research topic
- Descriptive title of the proposed research

- Name, address, and telephone number of the contact PD/PI
- Name of other key personnel
- Participating institutions
- Number and title of this notice of funding opportunity announcement (NOFO)

The letter of intent should be sent electronically to:

Mikel Walters, PhD
Scientific Review Official
Extramural Research Program Operations
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention (CDC)
Email: mwalters@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 at How to Apply - Application Guide 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 at How to Apply - Application Guide 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).

CDC OMB approved templates may be used (e.g. NCCDPHP template https://www.cdc.gov/chronicdisease/pdf/nofo/DMP-Template-508.docx)

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

Applicants must use FORMS-G application packages for due dates on or after April 4, 2022 and must use FORMS-F application packages until April 3, 2022.

Application guides for FORMS-F and FORMS-G application packages are posted to the How to Apply - Application Guide page.

Please use the form and instructions for SF424 (R&R) Form F. Applicants must use FORMS-F application packages until April 3, 2022.

6. Appendix

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

Up to 5 PDF files of supporting materials for the Research Plan may also be included in the appendix as described below (7. Page Limitations). The appendix has a total maximum page limit of 25 pages.

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

8. Format for Attachments

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

CDC requires all text attachments to the Adobe application forms be submitted as PDFs and that all text attachments conform to the agency-specific formatting requirements noted in the SF424 (R&R) Application Guide at .How to Apply - Application Guide.

Applicants must use FORMS-G application packages for due dates on or after April 4, 2022 and must use FORMS-F application packages until April 3, 2022.

Application guides for FORMS-F and FORMS-G application packages are posted to the How to Apply - Application Guide page.

Please use the form and instructions for SF424 (R&R) Form F. Applicants must use FORMS-F application packages until April 3, 2022.

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. Applicants will use a platform or system to submit applications.

ASSIST is a commonly used platform because it provides a validation of all requirements prior to submission. If ASSIST detects errors, then the applicant must correct errors before their application can be submitted. Applicants should view their applications 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 must be 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 02/24/2022

02/24/2022
Electronically submitted applications must be submitted no later than 5:00 p.m., ET, on the listed application due date.

10. 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, in 45 CFR Part 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.

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

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 (45 CFR 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.

Protection of Human Subjects and Personally Identifiable Information
The Research Strategy section of the application is expected to clearly describe the type, source, access to, and protections of the data and human subjects participating in the study. Access to non-publicly available, previously collected data must be clearly described in the Research Strategy and documented with a signed Data Sharing Agreement or Letter of Support. Access to publicly available, previously collected data must be clearly described in the Research Strategy.

Protection of previously collected data includes, but is not limited to, protection of personally identifiable information from loss and/or misuse.

The application is expected to identify each performance site that will be conducting human subjects research and include the FWA number for the applicant institution and each performance site. Research conducted with more than one institution will be expected to use a single Institutional Review Board (sIRB) to conduct the ethical review required by HHS regulations. See *Section IV. Application and Submission Information, 10 Funding Restrictions, Human Subjects* for details.

Data Management Plan
Applicants should develop and include, as part of the application's Resource Sharing Plan section of the PHS 398 Research Plan Component, a data management plan that meets the requirements of AR-25 using their own template. Applicants funded under this NOFO will be required to use NCIPC's Data Management Plan Template, OMB NO: 0920-1301 (Exp. Date: 06/30/2023) to make revisions to the DMP as required during the award's project period.

11. 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. 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 (http://grants.nih.gov/grants/guide /url_ redirect.htm? id=11144).

Important reminders:
All Senior/Key Personnel (including any Program Directors/Principal Investigators (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.

It is also important to note that for multi-project applications, this requirement also applies to the individual components of the application and not to just the Overall component.

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.

PLEASE NOTE: For applications due on or after April 4, 2022, applicants must have a unique entity identifier (UEI) at the time of application submission. In preparation for the federal government's April 4, 2022, transition from the Data Universal Numbering System (DUNS) to the Unique Entity Identifier (UEI), applicants must obtain a UEI. The UEI is generated as part of SAM.gov registration. Current SAM.gov registrants have already been assigned their UEI and can view it in SAM.gov and grants.gov. Additional information is available on the GSA website, SAM.gov, and Grants.gov-Finding the UEI.

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.d/////

Section V. Application Review Information

1. Criteria

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

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

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

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

To what extent will the proposed activities advance current knowledge and build the evidence base to better understand risk and protective factors for and patterns and trajectories of polydrug use and overdose?

To what extent will the proposed activities advance current knowledge and build the evidence base regarding use of polydrug combinations most likely to result in nonfatal overdose or death (such as combinations including synthetic opioids)?

To what extent does the applicant demonstrate how the proposed research can be used to inform focused drug use and overdose prevention efforts?

To what extent does the proposal focus on one of the following populations, 1) the general

population, and/or 2) persons who have experienced acute or chronic pain and used prescription opioids to manage their pain, and/or 3) or persons who use cannabis, either medically or non-medically and/or 4) other populations experiencing disproportionate burden of drug use and overdose (e.g., those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, sexual and gender minority groups, people with a history of substance use disorders and/or overdose)?

To what extent will the proposed project advance current knowledge and build the evidence base for populations experiencing disproportionate burden of polydrug use and overdose?

To what extent does the application propose research that will not be funded under this NOFO?

- Projects that do not propose to address the risk and protective factors, AND patterns, AND trajectories of polydrug use will not be recommended for funding;
- Projects that propose to primarily focus on alcohol or tobacco;
- Do not propose to focus on human subjects;
- Propose to focus on animal subjects.

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?

To what extent does the PI and Co-I Team have sufficient prior experience conducting research in the area of drug use or overdose, or related discipline consistent with what is proposed in the application?

To what extent does the PI/co-I Team have sufficient prior experience conducting research using the methods that are proposed in the application?

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?

To what extent are the proposed activities innovative yet balanced with a well described research strategy that is likely to be completed within the 3-year project period?

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?

To what extent does the research design adequately address each required research objective (evaluation of risk and protective factors for AND patterns of AND trajectories of polydrug use)?

To what extent is the application's proposed strategy adequately supported by theory or empirical evidence?

To what extent does the applicant propose using a rigorous design that includes data analytic plans appropriate to the research design and hypotheses?

To what extent does the applicant demonstrate how the approach will allow for the results to be used to inform focused drug use and overdose prevention efforts?

To what extent does the applicant adequately justify the selection of the study population(s)?

To what extent does the approach demonstrate use of data that is suitable for the research objective? Are these data appropriate for documenting the research outcome in the project period proposed for the study?

To what extent does the application's proposed strategy assure sample retention and adequate statistical power to produce meaningful results?

To what extent does the Research Strategy section of the application clearly describe the roles and responsibilities of each partner involved in the proposed study?

To what extent are the partnerships likely to result in a successful completion of the proposed research?

To what extent is the proposed study feasible and the timeline sufficiently detailed, complete and realistic for completing the proposed activities within the 3-year project period?

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?

Are the partnerships necessary and critical for successfully completing the research clearly described in the Research Strategy section of the application?

To what extent does the Research Strategy section of the application clearly describe the working relationships between the applicant institution and all partner organizations?

To what extent does the Research Strategy section of the application clearly describe the involvement and scope of work each partner is willing to complete to ensure the success of the proposed research within the proposed project period?

To what extent does the Research Strategy demonstrate access to the data, or include a plan for accessing the data, necessary to complete the proposed research within the proposed period of performance? To what extent does the Research Strategy demonstrate access to the proposed study participants?

To what extent are the relationships and activities of the partnerships described in the Research Strategy documented by a signed Data Sharing Agreement, Letter of Support, or Memorandum of Understanding that clearly delineates the intent and capabilities of each partnership?

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/additional-requirements/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://grants.nih.gov/grants/olaw/VAChecklist.pdf).

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

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

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

3. Additional Review Considerations

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

Applications from Foreign Organizations
N/A

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/additional-requirements/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.

CDC OMB approved templates may be used (e.g. NCCDPHP template https://www.cdc.gov/chronicdisease/pdf/nofo/DMP-Template-508.docx

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

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/application-resources.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 only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review), 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.
- Consideration for meritorious applications that include signed Data Sharing Agreements, Letters of Support, or Memorandum of Understanding for each partnership described in the Research Strategy section of the application.
- Consideration for meritorious applications that contribute to a diverse mix of strategies *to* improve our understanding of risk factors, patterns, and trajectories of polydrug use and overdose *across the general population as well as a diverse mix of key* subpopulations, including persons who have experienced acute or chronic pain and used prescription

opioids to manage their pain, persons who use cannabis, either medically or non-medically, or other subpopulations which have been disproportionately affected by overdose, as evidenced by the Research Strategy section of the application's research plan.

- Consideration for meritorious applications that propose to include communities experiencing a disproportionate burden of drug use and overdose, as evidenced by the Research Strategy section of the application's research plan.
    - These include, but are not limited to, those experiencing reduced economic stability; people experiencing homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, limited educational attainment, access or quality, limited healthcare access or quality, limited access to substance use treatment or limited health literacy; people with disabilities; people from non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minority groups, and sexual and gender minority groups to people with disabilities, non-English speaking populations, tribal populations, rural communities and other geographically underserved areas, racial/ethnic minorities, sexual and gender minorities, people with limited health literacy, people with a history of substance use disorders and/or overdose).
- Consideration for meritorious applications that contribute to a geographic balance of proposed projects, as evidenced by the congressional district of the applicant organization, to broaden the distribution of awards.
- Consideration for applicant organizations from or conducting research in collaboration or partnership with Minority Serving Educational Institutions (MSIs) i.e., Hispanic Serving Institutions (HSIs), Historically Black Colleges and Universities (HBCUs), Tribal Colleges and Universities (TCUs), or Alaska Native and Native Hawaiian Serving Institutions, as defined by the U.S. Department of Education, and as evidenced by MSI inclusion in the SF-424 Senior/Key Personnel form, to broaden distribution of awards.
- Consideration for applications in which the contact PD/PI meets NIH Early Stage Investigator (ESI) status, as verified by the NIH Determination of Investigator Status process, to broaden distribution of awards.
- Exclusion from funding consideration, regardless of the scientific or technical merit of the proposed project, as evidenced by the Research Strategy section of the application's research plan, of applications that:
    - Do not propose to address the risk and protective factors, AND patterns, AND trajectories of polydrug use will not be recommended for funding;
    - Propose to primarily focus on alcohol or tobacco;
    - Do not propose to focus on human subjects;
    - Propose to focus on animal subjects.

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 with 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 45 CFR Part 75, subpart F, 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).

PLEASE NOTE: For applications due on or after April 4, 2022, applicants must have a unique entity identifier (UEI) at the time of application submission. In preparation for the federal government's April 4, 2022, transition from the Data Universal Numbering System (DUNS) to the Unique Entity Identifier (UEI), applicants must obtain a UEI. The UEI is generated as part of SAM.gov registration. Current SAM.gov registrants have already been assigned their UEI and can view it in SAM.gov and grants.gov. Additional information is available on the GSA website, SAM.gov, and Grants.gov-Finding the UEI.

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/

Specific requirements that apply to this NOFO are the following:

AR-1: Human Subjects Requirements
AR-2: Requirements for Inclusion of Women and Racial and Ethnic Minorities in Research
AR-3: Animal Subjects Requirements
AR-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-17: Peer and Technical Reviews of Final Reports of Health Studies – ATSDR

AR-21: Small, Minority, And Women-owned Business
AR-22: Research Integrity
AR-24: Health Insurance Portability and Accountability Act Requirements
AR-25: Data Management and Access
AR-26: National Historic Preservation Act of 1966
AR-28: Inclusion of Persons Under the Age of 21 in Research
AR-29: Compliance with EO13513, "Federal Leadership on Reducing Text Messaging while Driving", October 1, 2009
AR-30: Information Letter 10-006, - Compliance with Section 508 of the Rehabilitation Act of 1973
AR-31: Research Definition
AR-32: Appropriations Act, General Provisions
AR-33: United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern
AR-34: Accessibility Provisions and Non-Discrimination Requirements
AR-36: Certificates of Confidentiality
AR-37: Prohibition on certain telecommunications and surveillance services or equipment for all awards issued on or after August 13, 2020.

Organization Specific ARs:
AR-8: Public Health System Reporting Requirements
AR-15: Proof of Non-profit Status
AR 23: Compliance with 45 C.F.R. Part 87

The full text of the Uniform Administrative Requirements, Cost Principles, and Audit Requirements for HHS Awards, 45 CFR 75, can be found at: https://www.ecfr.gov/cgi-bin/text-idx?node=pt45.1.75

To view brief descriptions of relevant CDC requirements visit: https://www.cdc.gov/grants/additionalrequirements/index.html

Additional CDC Award Requirements

The following Additional Requirements, some of which emphasize and expand upon those above, will be required for all recipients funded under this NOFO.

All award recipients under this NOFO will be required to complete pre-registration of the research project(s) using publicly available platforms or ClinicalTrials.gov as applicable, consistent with the National Science Foundation's open science principles. The platform for intended pre-registration should be described in the Research Plan at the time of application.

All award recipients under this NOFO will be required to make data publicly available within 30 months of completing data collection, this includes making source code available to the public, and ensuring open access to research publications consistent with the

National Science Foundation's open science principle.

The CDC will follow established implementation schedules and procedures for making grant awards under this NOFO in accordance with HHS and CDC Policy for Grant Program Administration and CDC Policy for Peer Review of Research and Scientific Programs to ensure that these awards support ideologically and politically unbiased research projects.

Data Management Plan. Applicants should develop and include, as part of the application's Resource Sharing Plan section of the PHS 398 Research Plan Component, a data management plan that meets the requirements of AR-25 using their own template. Applicants funded under this NOFO will be required to use NCIPC's Data Management Plan Template, OMB NO: 0920-1301 (Exp. Date: 06/30/2023) to make revisions to the DMP as required during the award's project period.

3. Additional Policy Requirements

The following are additional policy requirements relevant to this NOFO:

Should you successfully compete for an award, recipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age and, in some circumstances, religion, conscience, and sex (including gender identity, sexual orientation, and pregnancy).This includes taking reasonable steps to provide meaningful access to persons with limited English proficiency and providing programs that are accessible to and usable by persons with disabilities. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. See https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html and https://www.hhs.gov/civil-rights/for-individuals/nondiscrimination/index.html.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. For guidance on meeting your legal obligation to take reasonable steps to ensure meaningful access to your programs or activities by limited English proficient individuals, see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html and https://www.lep.gov.
- For information on your specific legal obligations for serving qualified individuals with disabilities, including providing program access, reasonable modifications, and taking appropriate steps to provide effective communication, see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html.
- HHS funded health and education programs must be administered in an environment free of sexual harassment, see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html.
- For guidance on administering your project in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-

discrimination laws, see https://www.hhs.gov/conscience/conscience-protections/index.html and https://www.hhs.gov/conscience/religious-freedom/index.html.

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 applies to all new obligations and all funds appropriated by Congress. For more information, visit the HHS website at: https://www.hhs.gov/grants/contracts/contract-policies-regulations/efficient-spending/index.html.

Federal Funding Accountability and Transparency Act of 2006 Federal Funding Accountability and Transparency Act of 2006 (FFATA), P.L. 109–282, as amended by section 6202 of P.L. 110–252, requires full disclosure of all entities and organizations receiving Federal funds including grants, contracts, loans and other assistance and payments through a single, publicly accessible website, www.usaspending.gov. For the full text of the requirements, please review the following website: https://www.fsrs.gov/.

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

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

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

The author's final, peer-reviewed manuscript is defined as the final version accepted for journal publication and includes all modifications from the publishing peer review process,

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

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

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

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

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

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

Data Management Plan(s)

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

findings, conclusions, and implementation.

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

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

Certificates of Confidentiality: Institutions and investigators are responsible for determining whether research they conduct is subject to Section 301(d) of the Public Health Service (PHS) Act. Section 301(d), as amended by Section 2012 of the 21st Century Cures Act, P.L. 114-255 (42 U.S.C. 241(d)), states that the Secretary shall issue Certificates of Confidentiality (Certificates) to persons engaged in biomedical, behavioral, clinical, or other research activities in which identifiable, sensitive information is collected. In furtherance of this provision, CDC-supported research commenced or ongoing after December 13, 2016 in which identifiable, sensitive information is collected, as defined by Section 301(d), is deemed issued a Certificate and therefore required to protect the privacy of individuals who are subjects of such research. Certificates issued in this manner will not be issued as a separate document, but are issued by application of this term and condition to this award. See Additional Requirement 36 to ensure compliance with this term and condition. The link to the full text is at: https://www.cdc.gov/grants/additional-requirements/ar-36.html.

4. Cooperative Agreement Terms and Conditions

N/A

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).

Technical Review and Summary Statement Response Requirements
Recipients will be required to electronically submit a response to the peer reviewers' comments and/or concerns, as documented in the Summary Statement, within 30 days of the notification of their initial award. Recipients will also be required to electronically submit a response to any progress concerns or areas for improvement noted on their annual Technical Review within the time period specified in the annual award continuation notice.

Annual Report Requirements
Recipients will be required to electronically submit an Annual Report within 90 to 120 days before the end of the current budget period. The Annual Report should include:

- A description of the completion status of each Specific Aim and/or research objective or milestone for the budget period.
- A complete list of the publications planned or completed to date - including status (e.g., published [include reference], in review, under development).
- A description of any changes made in the use of human subjects or IRB approval status.
- A description of any changes made in the Data Management Plan. Award recipients funded under this NOFO will be required to use NCIPC's Data Management Plan Template, OMB NO: 0920-1301 (Exp. Date: 06/30/2023) to make revisions to the DMP as required during the award's project period.

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 contribute 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:

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

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

The due date for final FFRs is 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 on the Payment Management System (PMS) can be found at https://pms.psc.gov.

Organizations may verify their current registration status by running the "List of Commons Registered Organizations" query found at: https://era.nih.gov/registration_accounts.cfm. Organizations not yet registered can go to https://commons.era.nih.gov/commons/ 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, healthcare 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.

6. Termination

CDC may impose other enforcement actions in accordance with 45 CFR 75.371- Remedies for Noncompliance, as appropriate.

The Federal award may be terminated in whole or in part as follows:

(1) By the HHS awarding agency or pass-through entity, if the non-Federal entity fails to comply with the terms and conditions of the award;

(2) By the HHS awarding agency or pass-through entity for cause;

(3) By the HHS awarding agency or pass-through entity with the consent of the non-Federal entity, in which case the two parties must agree upon the termination conditions, including the effective date and, in the case of partial termination, the portion to be terminated; or

(4) By the non-Federal entity upon sending to the HHS awarding agency or pass-through entity written notification setting forth the reasons for such termination, the effective date, and, in the case of partial termination, the portion to be terminated. However, if the HHS awarding agency or pass-through entity determines in the case of partial termination that the reduced or modified portion of the Federal award or subaward will not accomplish the purposes for which the Federal award was made, the HHS awarding agency or pass-through entity may terminate the Federal award in its entirety.

7. Reporting of Foreign Taxes (International/Foreign projects only)

A. Valued Added Tax (VAT) and Customs Duties – Customs and import duties, consular fees, customs surtax, valued added taxes, and other related charges are hereby authorized as an allowable cost for costs incurred for non-host governmental entities operating where no applicable tax exemption exists. This waiver does not apply to countries where a bilateral agreement (or similar legal document) is already in place providing applicable tax exemptions and it is not applicable to Ministries of Health. Successful applicants will receive information on VAT requirements via their Notice of Award.

B. The U.S. Department of State requires that agencies collect and report information on the amount of taxes assessed, reimbursed and not reimbursed by a foreign government against commodities financed with funds appropriated by the U.S. Department of State, Foreign Operations and Related Programs Appropriations Act (SFOAA) ("United States foreign assistance funds"). Outlined below are the specifics of this requirement:

1) Annual Report: The recipient must submit a report on or before November 16 for each foreign country on the amount of foreign taxes charged, as of September 30 of the same year, by a foreign government on commodity purchase transactions valued at 500 USD or more financed with United States foreign assistance funds under this grant during the prior United States fiscal year (October 1 – September 30), and the amount reimbursed and unreimbursed by the foreign government. [Reports are required even if the recipient did not pay any taxes during the reporting period.]

2) Quarterly Report: The recipient must quarterly submit a report on the amount of foreign taxes charged by a foreign government on commodity purchase transactions valued at 500 USD or more financed with United States foreign assistance funds under this grant. This report shall be submitted no later than two weeks following the end of each quarter: April 15, July 15, October 15 and January 15.

3) Terms: For purposes of this clause:

"Commodity" means any material, article, supplies, goods, or equipment;

"Foreign government" includes any foreign government entity;

"Foreign taxes" means value-added taxes and custom duties assessed by a foreign government on a commodity. It does not include foreign sales taxes.

4) Where: Submit the reports to the Director and Deputy Director of the CDC office in the country(ies) in which you are carrying out the activities associated with this cooperative agreement. In countries where there is no CDC office, send reports to VATreporting@cdc.gov.

5) Contents of Reports: The reports must contain:

a. recipient name;

b. contact name with phone, fax, and e-mail;

c. agreement number(s) if reporting by agreement(s);

d. reporting period;

e. amount of foreign taxes assessed by each foreign government;

f. amount of any foreign taxes reimbursed by each foreign government;

g. amount of foreign taxes unreimbursed by each foreign government.

6) Subagreements. The recipient must include this reporting requirement in all applicable subgrants and other subagreements.

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
Susan Neurath, PhD
National Center for Injury Prevention and Control (NCIPC)
Telephone: 770.488.3368
Email: SNeurath@cdc.gov

Peer Review Contact
Mikel Walters, Ph.D.
National Center for Injury Prevention and Control (NCIPC)
Telephone: 404.639.0913
Email: MWalters@cdc.gov

Financial/Grant Management Contact(s)
Manal Ali
Grants Management Specialist
CDC Office of Grants Services
Telephone: 770.488.2706
Email: HFO8@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 of Federal Regulations.

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

Successful recipients may be permitted expanded authorities in the administration of this award as provided for in the Code of Federal Regulations, Title 2, Subtitle A, Chapter II, Part 200, Subpart D, §200.308(d)(4). Specific authorities granted will be detailed in the official Notice of Award document.

Application Submission Process

Applications must be successfully submitted and complete all validation actions prior to 5PM ET of the application due date for this NOFO. Applicants are encouraged to submit the application in ASSIST three (3) business days before the stated due date to provide sufficient time to correct any errors. If post-submission errors are identified during the validation process, the errors must be corrected and the application must be re-submitted in ASSIST prior to 5PM ET of the application due date. 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.

Applicants who encounter problems when submitting their applications must attempt to resolve them by contacting the NIH eRA Service desk and the Grants.gov Contact Center. See *Section IV. Application and Submission Information, 9 Submission Dates & Times* for contact information.

General Information

All applications submitted for this NOFO must be responsive to the specific requirements and objectives of this NOFO and must be submitted as a new application through www.grants.gov.

All applicants are advised to carefully review the responsiveness requirements and

instructions on how applicants must document responsiveness in *Section III. Eligibility Information 5. Responsiveness* of this NOFO.

Applicants are encouraged to pay close attention to the Data Management Plan requirements.