

Centers for Disease Control and Prevention

National Center for Immunization and Respiratory Diseases Extramural Research Program Office

Research on the Epidemiology, Vaccine Effectiveness and Treatment of Influenza and Other Respiratory Viruses in Southeast Asia and the Western Pacific

RFA-IP-16-001

Application Due Date: 01/11/2016

Signature _____ Date _____

Research on the Epidemiology, Vaccine Effectiveness and Treatment of Influenza and Other Respiratory Viruses in Southeast Asia and the Western Pacific

RFA-IP-16-001

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Part 1. Overview Information

Participating Organization(s)

Centers for Disease Control and Prevention

Components of Participating Organizations

National Center for Immunization and Respiratory Diseases Extramural Research Program Office (NCIRD ERPO)
National Center for Immunization and Respiratory Diseases (NCIRD)

Funding Opportunity Announcement (FOA) Title

Research on the Epidemiology, Vaccine Effectiveness and Treatment of Influenza and Other Respiratory Viruses in Southeast Asia and the Western Pacific

Activity Code

U01 Research Project Cooperative Agreements

Funding Opportunity Announcement Type

New

Funding Opportunity Announcement Number

RFA-IP-16-001

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

93.083

Category of Funding Activity:

Health

FOA Purpose

The NCIRD Influenza Division (ID) is seeking a cooperative agreement with the School of Public Health, the University of Hong Kong (UHK), the Peoples' Republic of China to conduct research studies among older adults on the epidemiology and disease burden of influenza and other respiratory pathogens and to study alternative influenza vaccination strategies, including the relative efficacy of annual or twice-a-year vaccination for influenza. In addition, CDC seeks to collaborate with the UHK to conduct research studies among older adults on novel influenza viruses or other respiratory pathogens, including respiratory syncytial virus (RSV) infection. UHK has an established respiratory virus active surveillance system among older adults in a region of China with twice-yearly periods of influenza circulation which can be utilized to expand and conduct additional research on disease burden and vaccine efficacy in this population. This surveillance platform has allowed the research team at UHK to better understand risk factors for mild to severe influenza disease and its burden; however, it has not generated significant data on influenza vaccine efficacy among older adults. This new cooperative agreement will allow NCIRD ID to expand collaborations with UHK to examine this population in more depth as well as to better understand the best vaccine strategies for this age group and for regions with multiple or year-round epidemic periods. This cooperative agreement would build upon the existing surveillance system in China and the lessons learned from this system could be used in the future to establish a similar project in another country in the Asia-Pacific region.

Key Dates

Publication Date: **To receive notification of any changes to RFA-IP-16-001, return to the synopsis page of this announcement at www.grants.gov and click on the "Send Me Change Notification Emails" link. An email address is needed for this service.**

Letter of Intent Due Date: **N/A**

Application Due Date: **01/11/2016**

On-time submission requires that electronic applications be error-free and made available to CDC for processing from eRA Commons on or before the deadline date. Applications must be submitted to and validated successfully by Grants.gov/eRA Commons no later than 5:00 PM U.S. Eastern Time. Note: HHS/CDC grant submission procedures do not provide a period of time beyond the application due date to correct any error or warning notices of noncompliance with application instructions that are identified by Grants.gov or eRA systems (i.e., error correction window).

Scientific Merit Review: **03/17/2016**

Secondary Review: **04/07/2016**

Estimated Start Date: **08/01/2016**

Expiration Date: **01/12/2016**

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

Required Application Instructions

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

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

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

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

Executive Summary

- **Purpose:** The NCIRD Influenza Division (ID) is seeking a cooperative agreement with the School of Public Health, the University of Hong Kong (UHK), the Peoples' Republic of China to conduct research studies among older adults on the epidemiology and disease burden of influenza and other respiratory pathogens and to study alternative influenza vaccination strategies, including the relative efficacy of annual or twice a year vaccination for influenza. In addition, CDC seeks to collaborate with the UHK to conduct research studies among older adults on novel influenza viruses or other respiratory pathogens, including respiratory syncytial virus (RSV) infection. UHK has an established respiratory virus active surveillance system among older adults in a region of China with twice-yearly periods of influenza circulation which can be utilized to expand and conduct additional research on disease burden and vaccine efficacy in this population. This surveillance platform has allowed the research team at UHK to better understand risk factors for mild to severe influenza disease and its burden; however, it has not generated significant data on influenza vaccine efficacy among older adults. This new cooperative agreement will allow NCIRD ID to expand collaborations with UHK to examine this population in more depth as well as to better understand the best vaccine strategies for this age group and for regions with multiple or year-round epidemic periods. This cooperative agreement would build upon the existing surveillance system in China and the lessons learned from

this system could be used in the future to establish a similar project in another country in the Asia-Pacific region.

- **Mechanism of Support.** Cooperative Agreement
- **Funds Available and Anticipated Number of Awards.** Estimated total funding available including direct and indirect costs for the entire project period is $3,000,000 per year. The project period will be 5 years. There will be one award. The total amount awarded will depend upon the availability of funds and receiving a sufficiently meritorious application.
- **Budget and Project Period.** The estimated budget for the first year of this cooperative agreement is $3,000,000. The estimated total funding for the entire project period is up to $15,000,000 for the 5-year project period. The estimated project period for this cooperative agreement is 08/01/2016 to 07/31/2021.
- **Application Research Strategy Length:** Page limits for the Research Strategy component of the Resaerch Plan are clearly specified in Section IV. "Application and Submission Information" of this announcement.
- **Eligible Institutions/Organizations.** Institutions/organizations listed in Section III.1 are eligible to apply.
- **Eligible Project Directors/Principal Investigators (PDs/PIs).** Individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution/organization to develop an application for support. NOTE: CDC does not make awards to individuals directly. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply.
- **Number of PDs/PIs.** There will only be one PD/PI for this project.
- **Number of Applications.** The eligible applicant institution may submit only one application.
- **Application Type.** New
- **Special Date(s). N/A**
- **Application Materials.** See **Section IV.1** for application materials. Please note that Form C is to be used when downloading the application package: http://grants.nih.gov/grants/funding/424/SF424_RR_Guide_General_VerC.pdf
- **Hearing Impaired.** Telecommunications for the hearing impaired are available at: TTY: (770) 488-2783.

Part 2. Full Text

Section I. Funding Opportunity Description

Statutory Authority

Public Health Service Act 307; 42 U.S.C. 242l

1. Background and Purpose

Influenza vaccines are the most effective available tools to prevent influenza illness and secondary complications. Randomized controlled trials examining influenza vaccine efficacy and observational studies of influenza vaccine effectiveness (VE) to date indicate that inactivated influenza vaccines (IIV) are moderately effective in preventing influenza illness among all age groups (4); however, there are multiple gaps in our knowledge regarding influenza vaccine efficacy or effectiveness or the best vaccination strategies for older adults.

First, there is limited high quality data on influenza vaccine efficacy or effectiveness for older adults. The only large randomized placebo-controlled efficacy trial conducted among community-dwelling persons aged ≥60 years reported a vaccine efficacy of 58% (95% CI, 26%–77%) against serologically-confirmed symptomatic influenza illness during a season when the vaccine strains were considered to be well-matched to circulating strains (5). However, the validity of using serologic outcomes in vaccine trials has been

questioned (4). The results of observational studies on influenza vaccines among older adults are of variable quality and can be difficult to interpret (5-12). A 2010 Cochrane review by Jefferson *et al*. (13) and the reanalysis of the Cochrane review by Beyer *et al*. (14) did not reach agreement regarding the effectiveness of influenza vaccines for people aged 65 years or older. Further vaccine efficacy studies among older adults are challenging because random allocation to influenza vaccine or placebo is no longer ethically acceptable in the United States and in many other countries given international recommendations of annual vaccination for all older adults.

Second, there are gaps in our knowledge regarding how underlying health, frailty, and other correlates of aging may impact vaccine efficacy or effectiveness, including through humoral- and cell- mediated immune response to inactivated influenza vaccine (IIV) and the waning of protection over time (15-17).

Third, strategies to improve immunogenicity and VE among older adults are also unclear. Although recent studies indicate that a high antigen dose of IIV may improve VE (18), some studies, especially with non-human animals, suggest providing a booster dose of IIV months after an initial dose may improve immunogenicity for some vaccine strains. In contrast, other studies have observed reduced immunogenicity and VE after repeated annual IIV vaccinations, and the effect of prior vaccination on VE is poorly understood (19).

Fourth, more research is needed to identify the most appropriate influenza vaccination strategy in regions with twice-annual or year-round circulation of influenza. China is located across temperate and subtropical regions with complicated seasonal patterns of influenza transmission. Currently, mainland China follows the vaccination schedule recommended for the Northern Hemisphere countries, with annual campaigns starting in October. However, a recent study identified three epidemiological regions in China that are characterized by distinctly different influenza seasonality. Findings from this study indicate that Northern provinces (latitudes ≥33º N) experience winter epidemics, Southern provinces (latitude <27º N) experience peak activity in the spring and summer, whereas provinces at intermediate latitudes experience twice-annual influenza epidemics (20). This study suggests that region-specific influenza vaccination strategies may be warranted in China.

NCIRD's Influenza Division has partnered with the UHK School of Public Health in a previous collaboration in 2015 to establish a respiratory infection surveillance cohort of older adults in China. This FOA will build upon the existing capacity to further develop research collaborations in order to address multiple gaps in our knowledge of influenza VE among older adults.

This FOA is to support an evaluation of vaccine immunogenicity and relative efficacy of twice annual vaccination with IIV (administered in the Fall and Spring months) in a location with at least twice-annual influenza epidemics among older adults (defined as individuals aged 60-89 years at the time of enrollment) compared to those who receive a single IIV dose either in the Fall or Spring months. This FOA will support active surveillance of respiratory diseases within an observational cohort of older adults in order to assess the incidence of influenza illness among older adults who are either unvaccinated or receive influenza vaccine according to local standards of medical practice.

Healthy People 2020 and other National Strategic Priorities

Healthy People 2020 requirements do not apply to foreign entities.

Public Health Impact

The knowledge acquired from the proposed studies under this FOA should allow countries to understand both the burden of influenza illness and influenza vaccine efficacy among older adults, both of which are critical to informing national vaccination policies for this age group. In addition, countries that experience a twice-annual influenza epidemic could utilize this information to determine optimal timing of influenza vaccination, the utility of implementing twice-annual vaccination recommendations, or the relative preventive value of the Northern versus the Southern Hemisphere vaccine regimen in similar regions.

Relevant Work

1. Thompson WW, Shay DK, Weintraub E, *et al*. Influenza-associated hospitalizations in the United States. JAMA. 2004; 292(11):1333-1340.

2. Feng L, Shay DK, Jiang Y, et al. Influenza-associated mortality in temperate and subtropical Chinese cities, 2003-2008. Bulletin of the World Health Organization. Apr 1 2012; 90(4):279-288B.

3. Dawood FS, Iuliano AD, Reed C, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis. Sep 2012; 12(9):687-695.

4. Osterholm MT, Kelley NS, Sommer A, Belongia EA. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. Lancet Infect Dis. Jan 2012; 12(1):36-44.

5. Govaert TM, Thijs CT, Masurel N, Sprenger MJ, Dinant GJ, Knottnerus JA. The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial. JAMA. Dec 7 1994; 272(21):1661-1665.

6. Allsup S, Haycox A, Regan M, Gosney M. Is influenza vaccination cost effective for healthy people between ages 65 and 74 years? A randomised controlled trial. Vaccine. Dec 16 2004; 23(5):639-645.

7. Praditsuwan R, Assantachai P, Wasi C, Puthavatana P, Kositanont U. The efficacy and effectiveness of influenza vaccination among Thai elderly persons living in the community. J Med Assoc Thai. Feb 2005; 88(2):256-264.

8. Chen Q, Griffin MR, Nian H, *et al*. Influenza vaccine prevents medically attended influenza-associated acute respiratory illness in adults aged >/=50 years. The Journal of Infectious Diseases. Apr 1 2015; 211(7):1045-1050.

9. Jackson LA, Jackson ML, Nelson JC, Neuzil KM, Weiss NS. Evidence of bias in estimates of influenza vaccine effectiveness in seniors. International Journal of Epidemiology. Apr 2006; 35(2):337-344.

10.Jackson ML, Nelson JC, Weiss NS, Neuzil KM, Barlow W, Jackson LA. Influenza vaccination and risk of community-acquired pneumonia in immunocompetent elderly people: a population-based, nested case-control study. Lancet. Aug 2 2008; 372(9636):398-405.

11. Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the community-dwelling elderly. N Engl J Med. Oct 4 2007; 357(14):1373-1381.

12. Wong K, Campitelli MA, Stukel TA, Kwong JC. Estimating influenza vaccine effectiveness in community-dwelling elderly patients using the instrumental variable analysis method. Archives of Internal Medicine. Mar 26 2012; 172(6):484-491.

13. Jefferson T, Di Pietrantonj C, Al-Ansary LA, Ferroni E, Thorning S, Thomas RE. Vaccines for preventing influenza in the elderly. Cochrane Database Syst Rev. 2010(2):CD004876.

14. Beyer WE, McElhaney J, Smith DJ, Monto AS, Nguyen-Van-Tam JS, Osterhaus AD. Cochrane re-arranged: support for policies to vaccinate elderly people against influenza. Vaccine. Dec 5 2013; 31(50):6030-6033.

15. Goodwin K, Viboud C, Simonsen L. Antibody response to influenza vaccination in the elderly: a quantitative review. Vaccine. Feb 20 2006; 24(8):1159-1169.

16. Jackson LA, Nelson JC, Benson P, *et al*. Functional status is a confounder of the association of influenza vaccine and risk of all cause mortality in seniors. International Journal of Epidemiology. Apr 2006; 35(2):345-352.

17. Yao X, Hamilton RG, Weng NP, *et al*. Frailty is associated with impairment of vaccine-induced antibody response and increase in post-vaccination influenza infection in community-dwelling older adults. Vaccine.

Jul 12 2011; 29(31):5015-5021.

18. DiazGranados CA, Dunning AJ, Kimmel M, *et al*. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. N Engl J Med. Aug 14 2014; 371(7):635-645.

19. McLean HQ, Thompson MG, Sundaram ME, *et al*. Impact of repeated vaccination on vaccine effectiveness against influenza A(H3N2) and B during 8 seasons. Clinical Infectious Diseases: an official publication of the Infectious Diseases Society of America. Nov 15 2014; 59(10):1375-1385.

20. Yu H, Alonso WJ, Feng L, *et al*. Characterization of regional influenza seasonality patterns in China and implications for vaccination strategies: spatio-temporal modeling of surveillance data. PLoS Med. Nov 2013; 10(11):e1001552.

2. Approach

Objectives/Outcomes

Whenever possible, applications should include objectives written in the SMART format (e.g., Specific, Measurable, Achievable, Realistic and Time-bound).

Primary objectives:

- To investigate alternative influenza vaccination strategies for older adults;

- To determine the relative efficacy of twice-annual vaccination versus once-annual vaccination in preventing laboratory-confirmed influenza illness among adults aged 60-89 years in a location with twice-annual epidemics;

- To compare the relative efficacy of providing a single dose of inactivated influenza vaccine (IIV) using the Southern versus the Northern Hemisphere schedule in preventing influenza illness;

- To compare immune response to influenza vaccination among those receiving twice-annual versus annual vaccination;

- To compare the incidence of laboratory-confirmed influenza illness among those who receive IIV (annually or twice-annually) as part of the study versus among older adults in an observational cohort who receive standard local care in a region with little vaccination of older adults.

Secondary objectives:

- To assess the burden of medically-attended and non-medically attended laboratory-confirmed influenza illness among an observational cohort of older adults;

- To estimate the incidence of other respiratory pathogen infections, including respiratory syncytial virus (RSV), associated with acute illness among older adults during periods of local influenza circulation;

- To examine the immune response to repeated influenza vaccinations over multiple years in this older adult age group;

- To compare the immune response to influenza virus illness versus influenza vaccination;

- To evaluate the impact of influenza illness on functional decline in older adults and to evaluate influenza vaccine efficacy in preventing functional decline among older adults;

- To determine whether influenza vaccination reduces the severity of influenza illness among older adults who are infected with influenza despite vaccination;

- To examine the socio-demographic, health, environmental, and immune factors associated with primary or secondary influenza vaccine failure;

- To examine the association between infections with influenza viruses and other pathogens with biomarkers for illness severity;

- To assess risk factors for laboratory-confirmed influenza virus infection among older adults.

Target Population

Target populations for research activities include, but are not limited to, older adults (60-89 years of age at the time of enrollment) living in Southeast Asia or the Western Pacific regions.

Collaboration/Partnerships

Collaborations with others working in areas of respiratory viruses or vaccine effectiveness in Southeast Asia or the Western Pacific are encouraged. Collaborations with provincial and local public health agencies, as appropriate, are also encouraged. Collaborations with CDC Divisions working in these topic areas are also encouraged.

Evaluation/Performance Measurement

As part of the application, the PI must include measurable goals and aims based on a five-year research project period. The applicant will collaborate with CDC to: (1) establish specific, measurable, achievable, realistic and time-phased (SMART) project objectives for each activity described in the applicant's project plan, and (2) develop and implement project performance measures that are based on specific programmatic objectives. The application should develop a timeline to achieve study milestones and develop metrics to monitor the project's performance and progress. Also, the awardee must submit an annual progress report and an annual budget period progress report for their activities and outcomes based on their overall research goals and timeline. Please see Section VI. Award Administration Information of this FOA for more information on reporting requirements.

Translation Plan

The applicant should arrange quarterly meetings with appropriate partners in the areas and countries who will be collaborating under this FOA to discuss research progress and findings. The applicant is requested to identify topics for two manuscripts per year of funding and may include manuscripts for which funding was initiated prior to this cooperative agreement. Likewise, the results of this research should be presented at international conferences and published in peer-reviewed journals.

Section II. Award Information

Funding Instrument Type: Cooperative Agreement

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

Application Types Allowed:

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

Estimated Total Funding: $15,000,000

Estimated total funding available for the first year: $3,000,000

Estimated total funding available for the entire five-year project period: $15,000,000

Anticipated Number of Awards: 1

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

Award Ceiling: $3,000,000 Per Budget Period

Award Floor: $750,000 Per Budget Period

Total Project Period Length: 5 year(s)

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

HHS/CDC grants policies as described in the HHS Grants Policy Statement (http://www.hhs.gov/asfr/ogapa/aboutog/hhsgps107.pdf) will apply to the applications submitted and awards made in response to this FOA.

Section III. Eligibility Information

1. Eligible Applicants

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

2. Foreign Organizations

Foreign Organizations are eligible to apply.

Foreign (non-US) organizations must follow policies described in the HHS Grants Policy Statement (http://www.hhs.gov/asfr/ogapa/aboutog/hhsgps107.pdf), and procedures for foreign organizations described throughout the SF424 (R&R) Application Guide. International registrants can confirm DUNS by sending an e-mail to ccrhelp@dnb.com, including Company Name, D-U-N-S Number, and Physical Address, and Country. Special Instructions for acquiring a Commercial and Governmental Entity (NCAGE) Code: https://eportal.nspa.nato.int/AC135Public/Docs/US%20Instructions%20for%20NSPA%20NCAGE.pdf.

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

For this announcement, applicants may include collaborators or consultants from foreign institutions. All applicable federal laws and policies apply.

3. Special Eligibility Requirements

Additional Information on Eligibility

Single-Source Competition

University of Hong Kong, School of Public Health

Division of Epidemiology and Biostatistics

Applications submitted under this funding opportunity announcement must not include activities that overlap with simultaneously-funded research under other awards.

4. Justification for Less than Maximum Competition

Additional Information on Eligibility

Eligibility is limited to the Division of Epidemiology and Biostatistics of the School of Public Health, University of Hong Kong (UHK), Hong Kong, Peoples' Republic of China. It is the only advanced research and public health institute with the research and laboratory capacity to conduct an influenza vaccine trial that has also conducted research with a large cohort of older adults in a region with influenza circulation patterns appropriate for the study objectives.

Specifically:

-- The School of Public Health at UHK has established an observational cohort of older adults to monitor the occurrence of illness due to respiratory virus infections in a region of China with multiple periods of influenza circulation each year. This existing cohort can be accessed for the proposed study to aid in addressing CDC's objective to better understand the burden of influenza among older adults.

-- It is in the best interest of CDC to award the cooperative agreement to UHK since the existing recruitment procedures and data systems established for the observational cohort can be applied to the proposed vaccine trial, resulting in substantial cost and time savings for the government.

-- The existing cohort is located in an ideal region for a vaccine trial that intends to compare alternative vaccination schedules and consider the relative protective value of Northern and Southern Hemisphere vaccines.

-- The School of Public Health, UHK, possesses the necessary scientific and managerial capacity for this study and has successfully completed a cooperative agreement with the influenza division related to the 2009 H1N1 influenza pandemic.

-- The research team at the School of Public Health, UHK has experience conducting randomized placebo-controlled trials and other influenza vaccine studies. This expertise is crucial to the success of this cooperative agreement. No other acceptable setting has been identified.

5. Responsiveness

N/A

6. Required Registrations

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

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

All applicant organizations must register with **Grants.gov**. Please visit www.Grants.gov at least 30 days prior to submitting your application to familiarize yourself with the registration and submission processes. The "one-time" registration process will take three to five days to complete. However, it is best to start the registration process at least two weeks prior to application submission.
All Program Directors/Principal Investigators (PD/PIs) **must** also work with their institutional officials to register with the **eRA Commons** or ensure their existing eRA Commons account is affiliated with the eRA

Commons account of the applicant organization. **All registrations must be successfully completed and active before the application due date**. Applicant organizations are strongly encouraged to start the registration process at least four (4) weeks prior to the application due date.

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

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

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

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

9. Cost Sharing

This FOA does not require cost sharing as defined in the HHS Grants Policy Statement (http:// www.hhs.gov/ asfr/ ogapa/ aboutog/ hhsgps107.pdf).

10. Number of Applications

As defined in the HHS Grants Policy Statement, (http: //www.hhs.gov /asfr /ogapa /aboutog /hhsgps107. pdf), applications received in response to the same funding opportunity announcement 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 FOA that is essentially the same as one currently pending initial peer review unless the applicant withdraws the pending application.

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

Section IV. Application and Submission Information

1. Address to Request Application Package

Applicants must download the SF424 (R&R) application package associated with this funding opportunity from www.Grants.gov.
If access to the Internet is not available or if the applicant encounters difficulty accessing the forms on-line, contact the HHS/CDC Procurement and Grants Office Technical Information Management Section (PGO TIMS) staff at (770) 488-2700 or pgotim@cdc.gov for further instructions. Hours: Monday - Friday, 7am –

4:30pm U.S. Eastern Standard Time. CDC Telecommunications for the hearing impaired or disabled is available at: TTY 1-888-232-6348.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the SF424 (R&R) Application Guide (http://grants.nih.gov/grants/funding/ 424/SF424_RR_Guide_General_VerC.pdf), except where instructed in this Funding Opportunity Announcement to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

The forms package associated with this FOA includes all applicable components, mandatory and optional. Please note that some components marked optional in the application package are required for submission of applications for this FOA. Follow the instructions in the SF 424 (R&R) Application Guide to ensure you complete all appropriate "optional" components.

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

3. Letter of Intent

Due Date for Letter of Intent:

N/A

4. Required and Optional Components

A complete application has many components, both required and optional. The forms package associated with this FOA in Grants.gov includes all applicable components for this FOA, required and optional.

5. PHS 398 Research Plan Component

The SF424 (R&R) Application Guide includes instructions for applicants to complete a PHS 398 Research Plan that consists of 16 components. Not all 16 components of the Research Plan apply to all Funding Opportunity Announcements (FOAs). Specifically, some of the following 16 components are for Resubmissions or Revisions only. See Part I, Section 5.5 of the SF 424 (R&R) Application Guide (http://grants.nih.gov/grants/funding/424/SF424_RR_Guide_General_VerC.pdf) for additional information. Please attach applicable sections of the following Research Plan components as directed in Part 2, Section 1 (Funding Opportunity Announcement Description).

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

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

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

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

4. Inclusion Enrollment Report (Renewal and Revision applications ONLY)

5. Progress Report Publication List (for Continuation ONLY)

Human Subjects Section

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

Other Research Plan Sections

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

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

6. Appendix

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

7. Page Limitations

All page limitations described in this individual FOA must be followed. For this specific FOA, the Research Strategy component of the Research Plan narrative is limited to 25 pages. Supporting materials for the Research Plan narrative included as appendices may not exceed 10 PDF files with a maximum of 50 pages for all appendices.

8. Format for Attachments

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

CDC requires all text attachments to the Adobe application forms be submitted as PDFs and that all text attachments conform to the agency-specific formatting requirements noted in the SF424 (R&R) Application Guide (Part I, Section 2) (http://grants.nih.gov/ grants/funding/424/ SF424_RR_Guide_General_VerC.pdf).

9. Submission Dates & Times

Part I. Overview Information contains information about Key Dates. Applicants are encouraged to submit in advance of the deadline to ensure they have time to make any application corrections that might be necessary for successful submission.

Organizations must submit applications via Grants.gov (http://www.grants.gov), the online portal to find and apply for grants across all Federal agencies. The eRA Commons systems retrieve the application from Grants.gov and check the application against CDC business rules. If no errors are found, the application will be assembled in the eRA Commons for viewing by the applicant before moving on for further CDC processing.

If errors are found, the applicant will be notified in the eRA Commons. They must make required changes to the local copy of their application and submit again through Grants.gov.

Applicants are responsible for viewing their application in the eRA Commons to ensure accurate and successful submission.

Once you can see your application in the Commons, be sure to review it carefully as this is what the reviewer will see. Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (http:// grants.nih. gov/grants /guide/url_redirect .htm? id=11123).

Information on the submission process is provided in the SF424 (R&R) Application Guide.

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

The application package is not complete until it has passed the Grants.gov/eRA Commons validation process. This process and email notifications of receipt, validation or rejection may take two (2) business days.

Applicants are strongly encouraged to allocate additional time prior to the submission deadline to submit their applications and to correct errors identified in the validation process. Applicants are encouraged also to check the status of their application submission to determine if the application packages are complete and error-free. Applicants who encounter system errors when submitting their applications must attempt to resolve them by contacting the Grants.gov Contact Center (1-800-518-4726; support@grants.gov). If the system errors cannot be resolved, applicants must contact CDC PGO TIMS at 770-488-2700; pgotim@cdc.gov for guidance at least 3 calendar days before the deadline date.

After submission of your application package, applicants will receive a "submission receipt" email generated by Grants.gov. Grants.gov will then generate a second e-mail message to applicants which will either validate or reject their submitted application package. This validation process may take as long as two (2) business days. A third and final e-mail message is generated once the applicant's application package has passed validation and the grantor has confirmed receipt of the application.

Unsuccessful Submissions:
If an application submission was unsuccessful, ***the applicant*** must:
1. Track his/her submission and verify the submission status (tracking should be done initially regardless of rejection or success).
    a. If the status states "***rejected***," do #2a or #2b.
2. Check his/her emails from both Grants.gov and eRA Commons for rejection notices.
    a. If the deadline has passed, he/she should email the Grant Management Specialist listed in the FOA (pgotim@cdc.gov) explaining why the submission failed.
    b. If there is time before the deadline, he/she should correct the problem(s) and resubmit as soon as possible.

Due Date for Applications: **01/11/2016**

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

10. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review (http:// www. whitehouse.gov/ omb/ grants_spoc).

11. Funding Restrictions

All HHS/CDC awards are subject to the terms and conditions, cost principles, and other requirements described in the HHS Grants Policy Statement. Pre-award costs may be allowable as an expanded authority, but only if authorized by CDC.
For more information on expanded authority and pre-award costs, go to: http://www.hhs.gov/asfr/ogapa/aboutog/hhsgps107.pdf.

Funds related 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.

Projects that involve the collection of information, identical record keeping or reporting from 10 or more individuals and are funded by a cooperative agreement and constitute a burden of time, effort, and/or resources expended to collect and/or disclose the information will be subject to review and approval by the Office of Management and Budget (OMB) under the Paperwork Reduction Act (PRA).

On September 24, 2014, the Federal government issued a policy for the oversight of life sciences "Dual Use Research of Concern" (DURC) and required this policy to be implemented by September 24, 2015. This policy applies to all New and Renewal awards issued on applications submitted on or after September 24, 2015, and to all non-competing continuation awards issued on or after that date. CDC grantee institutions and their investigators conducting life sciences research subject to the Policy have a number of responsibilities that they must fulfill. Institutions should reference the policy, available at http://www.phe.gov/s3/dualuse, for a comprehensive listing of those requirements. Non-compliance with this Policy may result in suspension, limitation, or termination of United States Government (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.

12. Other Submission Requirements and Information

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

Important reminders:
All PD/PIs must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF 424(R&R) Application Package. Failure to register in the Commons and to

include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to CDC.

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

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

Section V. Application Review Information

1. Criteria

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

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

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

Significance

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

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?

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?

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?

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?

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.

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.

As part of the Biohazards assessment, reviewers will evaluate whether the research proposed qualifies as Dual Use Research of Concern. Despite its value and benefits, certain types of research conducted for legitimate purposes can be utilized for both benevolent and harmful purposes. Such research is called "dual use research." Dual use research of concern is a subset of dual use research defined as: "life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security." The United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern articulates the practices and procedures required to ensure that dual use research of concern is identified at the institutional level and risk mitigation measures are implemented as necessary. 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/Documents/durc-companion-guide.pdf.

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 (http://www.cdc.gov/od/pgo/funding/grants/additional_req.shtm#ar1).

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 (http://www.cdc.gov/maso/Policy/Policy_women.pdf and http://www.gpo.gov/fdsys/pkg/FR-1995-09-15/pdf/95-22950.pdf#page=1) and the policy on the Inclusion of Persons Under 21 in Research (http://www.cdc.gov/maso/Policy/policy496.pdf).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11150).

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.

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
Reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

Resource Sharing Plans
HHS/CDC policy requires that recipients of grant awards make research resources and data readily available for research purposes to qualified individuals within the scientific community after publication. Please see: http://www.cdc.gov/grants/additionalrequirements/index.html. Investigators responding to this funding opportunity should include a plan on sharing research resources and data.

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

4. Review and Selection Process

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

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

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

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

5. Anticipated Announcement and Award Dates

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

Section VI. Award Administration Information

1. Award Notices

Any applications awarded in response to this FOA 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 (http:// www.hhs.gov/ asfr/ogapa/aboutog/ hhsgps107.pdf).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the Grants Management Officer is the authorizing document

and will be sent via email to the grantee's business official.

Awardees 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

All HHS/CDC grant and cooperative agreement awards include the HHS Grants Policy Statement as part of the NoA. For these terms of award, see the HHS Grants Policy Statement Part II: Terms and Conditions of Award (http:// www.hhs.gov/ asfr/ogapa/ aboutog/ hhsgps107.pdf).

Awardees must comply with the administrative requirements (AR) outlined in 45 Code of Federal Regulations (CFR) Part 74 or Part 92, as appropriate, as well as any additional requirements included in the FOA.

Specific requirements that apply to this FOA are the following:

Generally applicable ARs:

AR-1: Human Subjects Requirements

AR-2: 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 2020

AR-12: Lobbying Restrictions

AR-14: Accounting System Requirements

AR-16: Security Clearance Requirement

AR-21: Small, Minority, And Women-owned Business

AR-22: Research Integrity

AR-24: Health Insurance Portability and Accountability Act Requirements

AR-25: Release and Sharing of Data

AR-28: Inclusion of Persons Under the Age of 21 in Research

AR-29: Compliance with EO13513, “;Federal Leadership on Reducing Text Messaging while Driving”;, October 1, 2009

AR-30: Information Letter 10-006, - Compliance with Section 508 of the Rehabilitation Act of 1973

AR 31 - Distinguishing Public Health Research and Public Health Nonresearch

AR 32 –; FY 2012 Enacted General Provisions

For more information on the Code of Federal Regulations, visit the National Archives and Records Administration at: http://www.archives.gov/.

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

Additional Policy Requirements Relevant to this FOA:

Dual Use Research of Concern (DURC)

On September 24, 2014, the Federal government issued a policy for the oversight of life sciences "Dual Use Research of Concern" (United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern. September 24, 2014. Available at: http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf) and required this policy to be implemented by September 24, 2015. DURC is defined as life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security. The fundamental aim of this oversight policy is to preserve the benefits of life sciences research while minimizing the risk of misuse of the knowledge, information, products, or technologies provided by such research.

The DURC policy applies to recipients in the United States that receive Federal funding for life sciences research and that conduct or sponsor research involving one or more of the 15 agents or toxins listed in the policy. This policy also applies to foreign recipients that receive Federal funding to conduct or sponsor research involving one of these 15 agents or toxins. Research funded by CDC involving these agents or toxins 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 may be completed by an Institutional Review Entity (IRE) identified by the funded institution. Many institutions task their Institutional Biosafety Committees with this responsibility.

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 or cooperative agreement 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. For example, CDC may request that the institution periodically review a project for its DURC potential, propose any modifications to the risk mitigation plan, and share any resulting manuscripts with their Program Official prior to submitting the manuscript to a journal. CDC's Institutional Biosecurity Board (IBB) is responsible for approval of all DURC risk mitigation plans. The award recipient is responsible for adhering to the risk mitigation plan, as approved by CDC.

3. Additional Policy Requirements

The following are additional policy requirements relevant to this FOA:

HHS Policy on Promoting Efficient Spending: Use of Appropriated Funds for Conferences and Meetings, Food, Promotional Items and Printing Publications

This policy supports the Executive Order on Promoting Efficient Spending (EO 13589), the Executive Order on Delivering and Efficient, Effective, and Accountable Government (EO 13576) and the Office of Management and Budget Memorandum on Eliminating Excess Conference Spending and Promoting Efficiency in Government (M-35-11). This policy apply to all new obligations and all funds appropriated by Congress. For more information, visit the HHS website at: http:// www.hhs.gov/ asfr/ogapa/acquisition/ effspendpol_memo.html)

Federal Funding Accountability and Transparency Act of 2006

Public Law 109-282, the Federal Funding Accountability and Transparency Act of 2006 as amended (FFATA), 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 Web site, www.USASpending.gov (http:// 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 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.

Tobacco and Nutrition Policies
The CDC supports implementing evidence-based programs and policies to reduce tobacco use and secondhand smoke exposure, and to promote healthy nutrition. CDC encourages all awardees to implement the following *optional* evidence-based tobacco and nutrition policies within their organizations. These policies build on the current federal commitment to reduce exposure to secondhand smoke, which includes The Pro-Children Act, 20 U.S.C. 7181-7184 that prohibits smoking in certain facilities that receive federal funds.
Tobacco:

- Tobacco-free indoors – no use of any tobacco products (including smokeless tobacco) or electronic cigarettes in any indoor facilities under the control of the applicant.
- Tobacco-free indoors and in adjacent outdoor areas – no use of any tobacco products or electronic cigarettes in any indoor facilities, within 50 feet of doorways and air intake ducts, and in courtyards under the control of the applicant.
- Tobacco-free campus – no use of any tobacco products or electronic cigarettes in any indoor facilities and anywhere on grounds or in outdoor space under the control of the applicant.

Nutrition:

- Healthy food service guidelines that at a minimum align with Health and Human Services and General Services Administration Health and Sustainability Guidelines for Federal Concessions and Vending Operations for cafeterias, snack bars, and vending machines in any facility under the control of the recipient organization and in accordance with contractual obligations for these services. The following are resources for healthy eating and tobacco free workplaces:

  - http://www.gsa.gov/graphics/pbs/ Guidelines_for_Federal_Concessions_and_Vending_Operations.pdf
  - http://www.cdc.gov/ nccdphp/dnpao/hwi/toolkits/ tobacco/index.htm
  - http://www.cdc.gov/nutrition/index.html

Applicants should state whether they choose to participate in implementing these two optional policies. However, no applicants will be evaluated or scored on whether they choose to participate in implementing these optional policies.

4. Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and CDC grant administration policies.The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial CDC programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the HHS/CDC purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; CDC Project

Officers are not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and HHS/CDC as defined below.

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

- Ensuring the protection of human subjects through ethical review of all protocols involving human subjects at the local institution and at CDC and obtaining the appropriate Institutiional Review Board approvals for all institutions or individuals engaged in the conduct of the research project.
- Ensuring high quality data collection, quality assurance, and quality control procedures are in place for epidemiological and laboratory data.
- Communicating with the CDC Project Officer about research progress, budgetary changes, and upcoming deadlines for ethical review and abstract submission for international conferences.
- Working with CDC scientists to obtain OMB-PRA approvals, as needed.
- Complying with the responsibilities for the PI as described in the United States Government Policy for Institutional Oversight of Life Science Dual Use Research of Concern (DURC) http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf).
- Attending the annual PI meeting in Atlanta to discuss study progress, challenges, and next steps (include the cost of travel in the application's annual budgets).
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and CDC policies.
- Participating in routine conference calls to discuss study – initially, calls will be conducted on a biweekly basis and will revert to monthly calls when appropriate achievement is obtained.
- Allowing adequate time for CDC clearance of all manuscripts produced from this collaboration (at least 6 weeks).
- PUBLICATIONS: Publications, journal articles, etc. produced under a CDC grant support project must bear an acknowledgment and disclaimer, as appropriate, for example: "This publication (journal article, etc.) was supported by the Cooperative Agreement Number above from the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention". In addition, the PI/PD must provide to the CDC Project Officer the abstracts or manuscripts prior to any presentation or publication related to this funding for clearance and approval. The grantee will not seek to publish or present results or findings from this project without prior clearance and approval from CDC.

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

- Through regular communication, CDC Influenza staff will collaborate on conceptualization, design and implementation of the study and analysis, drafting and publication of results as warranted.
- Prepare and submit the paperwork necessary for research protocols to the CDC Institutional Review Board for review.
- Obtain Office of Management and Budget approval per the Paperwork Reduction Act, if necessary.
- Assist the PI, as needed, in complying with the PI responsibilities described in the United States Government Policy for Institutional Oversight of Life Science Dual Use Research of Concern (DURC) http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf

Areas of Joint Responsibilities include:

- Review and give scientific feedback on protocols, questionnaires, or other data collection instruments for cooperative agreement-supported studies and OMB-PRA clearance, as necessary.
- Prepare abstracts, manuscripts, and presentations of data collected from cooperative agreement-supported studies, as warranted.

- Mentor trainees, including EIS officers, fellows, and medical students.
- Collaborate in the development of human subjects research protocols and additional documents for IRB review by all cooperating institutions participating in the project and for OMB review, as needed.

Additionally, an agency Scientific Program Officer will be responsible for the normal scientific and programmatic stewardship of the award as described below:

- Named in the Notice of Award as the Program Official to provide overall scientific and programmatic stewardship of the award.
- Serve as the primary point of contact on official award-related activities, including an annual review of the grantee's performance as part of the request for continuation application.
- Make recommendations on requests for changes in scope, objectives, and or budgets that deviate from the approved peer-reviewed application.
- Carry out continuous review of all activities to ensure objectives are being met.
- Attend committee meetings and participate in conference calls for the purposes of assessing overall progress, and for program evaluation purposes.
- Monitor performance against approved project objectives.

5. Reporting

Awardees will be required to submit the Non-Competing Continuation Grant Progress Report (PHS 2590) annually 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 awardees 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 awardees of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All awardees 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 (http:// www.hhs.gov/asfr/ ogapa/aboutog/ hhsgps107.pdf) for additional information on this reporting requirement.

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**, (use form PHS 2590, posted on the HHS/CDC website, www.grants.gov and at http:// grants.nih.gov/grants/ funding/2590/ 2590.htm, **is due 90 to 120 days prior to the end of the current budget period.** 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 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 project period.**

B. Content of Reports

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

- Description of Progress during Annual Budget Period: Current Budget Period Progress reported on the PHS 2590 (http:// grants1.nih.gov/ grants/funding/ 2590/2590.htm) http:// grants.nih.gov/grants/ funding/2590/2590.htm: Detailed narrative report for the current budget period that directly addresses progress towards the Measures of Effectiveness included in the current budget period proposal.

- Research Aims: list each research aim/project

  a) Research Aim/Project: purpose, status (met, ongoing, and unmet), challenges, successes, and lessons learned
  b) Leadership/Partnership: list project collaborations and describe the role of external partners.

- Translation of Research (1 page maximum). When relevant to the goals of the research project, the PI should describe how the significant findings may be used to promote, enhance, or advance translation of the research into practice or may be used to inform public health policy. This section should be understandable to a variety of audiences, including policy makers, practitioners, public health programs, healthcare institutions, professional organizations, community groups, researchers, and other potential users. The PI should identify the research findings that were translated into public health policy or practice and how the findings have been or may be adopted in public health settings. Or, if they cannot be applied yet, this section should address which research findings may be translated, how these findings can guide future research or related activities, and recommendations for translation. If relevant, describe how the results of this project could be generalized to populations and communities outside of the study. *Questions to consider in preparing this section include*:

  - How will the scientific findings be translated into public health practice or inform public health policy?
  - How will the project improve or effect the translation of research findings into public health practice or inform policy?
  - How will the research findings help promote or accelerate the dissemination, implementation, or diffusion of improvements in public health programs or practices?
  - How will the findings advance or guide future research efforts or related activities?

- Public Health Relevance and Impact (1 page maximum). This section should address improvements in public health as measured by documented or anticipated outcomes from the project. The PI should consider how the findings of the project relate beyond the immediate study to improved practices, prevention or intervention techniques, inform policy, or use of technology in public health. *Questions to consider in preparing this section include*:

  - How will this project lead to improvements in public health?
  - How will the findings, results, or recommendations been used to influence practices, procedures, methodologies, etc.?
  - How will the findings, results, or recommendations contributed to documented or projected

reductions in morbidity, mortality, injury, disability, or disease?

- Current Budget Period Financial Progress: Status of obligation of current budget period funds and an estimate of unobligated funds projected provided on an estimated FFR.
- New Budget Period Proposal:
    - Detailed operational plan for continuing activities in the upcoming budget period, including updated Measures of Effectiveness for evaluating progress during the upcoming budget period. Report listed by Research Aim/Project.
    - Project Timeline: Include planned milestones for the upcoming year (be specific and provide deadlines).
- New Budget Period Budget: Detailed line-item budget and budget justification for the new budget period. Use the CDC budget guideline format.
- Publications/Presentations: Include publications/presentations resulting from this CDC grant only during this budget period. If no publication or presentations have been made at this stage in the project, simply indicate “Not applicable: No publications or presentations have been made."
- IRB Approval Certification: Include all current IRB approvals to avoid a funding restriction on your award. If the research does not involve human subjects, then please state so. Please provide a copy of the most recent local IRB and CDC IRB, if applicable. If any approval is still pending at time of APR due date, indicate the status in your narrative.

2. Annual Federal Financial Reporting

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

Failure to submit the required information in a timely manner may adversely affect the future funding of this project. If the information cannot be provided by the due date, you are required to submit a letter explaining the reason and date by which the Grants Officer will receive the information. **All CDC Financial Expenditure data due on/after October 1, 2012 must be submitted using the FFR via the eFSR/FFR system in the eRA Commons.** All Federal Reporting in the Payment Management System is unchanged. All new submissions should be prepared and submitted as FFRs.

CDC's implementation of the FFR retains a financial reporting period that coincides with the budget period of a particular project. However, **the due date for annual FFRs will be 90 days after the end of the calendar quarter in which the budget period ends**. Note that this is a change in due dates of annual FFRs and may provide up to 60 additional days to report, depending upon when the budget period end date falls within a calendar quarter. For example, if the budget period ends 1/30/2012, the annual FFR is due 6/30/2012 (90 days after the end of the calendar quarter of 3/31/2012). Due dates of final reports will remain unchanged. The due date for final FFRs will continue to be 90 days after the project period end date. Grantees must submit closeout reports in a timely manner. Unless the Grants Management Officer (GMO) of the awarding Institute or Center approves an extension, grantees 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 grantees are now available at http:// grants.nih.gov/ grants/forms.htm. For further information, contact GrantsInfo@nih.gov. Additional resources concerning the eFSR/FFR

system, including a User Guide and an on-line demonstration, can be found on the eRA Commons Support Page: http://www.cdc.gov/grants/interestedinapplying/applicationresources.html
FFR Submission: The submission of FFRs to CDC will require organizations to register with eRA Commons (Commons) (https://public.era.nih.gov/chl/public/search/commonsRegisteredOrgs.era). CDC recommends that this one time registration process be completed at least 2 weeks prior to the submittal date of a FFR submission.
Organizations may verify their current registration status by running the "List of Commons Registered Organizations" query found at: http://era.nih.gov/commons/. Organizations not yet registered can go to https:// commons. era.nih.gov/ commons/ registration/ registration Instructions. jsp 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: http:// era.nih.gov/ commons /index.cfm.

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 project period. 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.

Section VII. Agency Contacts

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

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

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

CDC Technical Information Management Section (TIMS)
Procurement and Grants Office
Telephone 770-488-2700
Email: PGOTIM@cdc.gov
Hours: Monday - Friday, 7am – 4:30pm U.S. Eastern Standard Time

Scientific Program/Research Contact:

Amy Yang, PhD

Office of the Associate Director for Science

National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention

United States Department of Health and Human Services

Centers for Disease Control and Prevention (CDC)

1600 Clifton Rd., NE, MS-E60

Atlanta, GA 30329-4027

Telephone: (404) 718-8834

Fax: (404) 718-8822

Email: vdz9@cdc.gov

Peer Review Contact:

Gregory Anderson, MPH, MS

Office of the Associate Director of Science

National Center for HIV/AID, Hepatitis and TB Prevention

United States Department of Health and Human Services

Centers for Disease Control and Prevention (CDC)

1600 Clifton Rd., NE, MS-E60

Atlanta, GA 30329-4027

Telephone: (404) 718-8833

Fax: (404) 718-8822

Email: gca5@cdc.gov

Financial/Grants Management Contact:

Dionne Bounds

Procurement and Grants Office (PGO)

Centers for Disease Control and Prevention (CDC)
2920 Brandywine Road
Atlanta, GA 30341-4146
Telephone: (770) 718-2082
Fax: (770) 488-2688
Email: vhv5@cdc.gov

Section VIII. Other Information

Other CDC funding opportunity announcements can be found at www.grants.gov.
All awards are subject to the terms and conditions, cost principles, and other considerations described in the HHS Grants Policy Statement.

Authority and Regulations
Awards are made under the authorization of Sections of the Public Health Service Act as amended and under the Code Federal Regulations.
Section 307 of the Public Health Service Act 42 U.S.C. 242l