

Centers for Disease Control and Prevention

National Center for Immunization and Respiratory Diseases Extramural Research Program Office

Annual Estimates of Influenza Vaccine Effectiveness for Preventing Medically Attended Laboratory-Confirmed Influenza in the United States

RFA-IP-16-002

Application Due Date: 01/11/2016

Annual Estimates of Influenza Vaccine Effectiveness for Preventing Medically Attended Laboratory-Confirmed Influenza in the United States

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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

Annual Estimates of Influenza Vaccine Effectiveness for Preventing Medically Attended Laboratory-Confirmed Influenza in the United States

Activity Code

U01 Research Project Cooperative Agreements

Funding Opportunity Announcement Type

New

Funding Opportunity Announcement Number

RFA-IP-16-002

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

93.185

Category of Funding Activity:

Health

FOA Purpose

The goal of this Funding Opportunity Announcement (FOA) is to support a network of US institutions that can obtain reliable vaccination information for a population and provide accurate estimates of annual influenza vaccine effectiveness (VE) to prevent influenza-associated illness in that population. Participating institutions will coordinate enrollment of patients with acute respiratory illness (ARI), confirm influenza infection using a standardized reverse-transcription PCR (RT-PCR) assay, and estimate VE using a test-negative study design. Interim VE estimates during the influenza season and end-of-season VE estimates will be used to inform vaccine recommendations and assess public health impact of influenza vaccination programs to prevent influenza-related illness and medical visits among persons of all ages. In addition, this network will compare VE for specific vaccine types available in the US. This network will serve as an emergency response resource in the event of an influenza pandemic to assess VE to prevent medically-attended illness associated with pandemic influenza.

NOTE: Section VIII. "Other Information" has been amended to include a "Summary of the Conference Call held on Thursday, December 3, 2015 with Potential Applicants" on pages 38-42.

Key Dates

Publication Date:	**To receive notification of any changes to RFA-IP-16-002, return to the synopsis page of this announcement at www.grants.gov and click on the "Send Me Change Notification Emails" link. An email address is needed for this service.**
Letter of Intent Due Date:	**12/14/2015**

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: **02/15/2016**

Secondary Review: **03/11/2016**

Estimated Start Date: **07/01/2016**

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

Due Dates for E.O. 12372: **Due no later than 60 days after the application receipt date.**

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.** Influenza is an important cause of morbidity, mortality, and healthcare burden across all age groups. Because influenza viruses are constantly changing and vaccines are reformulated every year, annual estimates of the effectiveness of influenza vaccines in preventing illness due to influenza infection and its associated complications are needed in order to evaluate the protection provided by annual, nationwide vaccination programs. The goal of this Funding Opportunity Announcement (FOA) is to support a network of US institutions that can obtain reliable vaccination information for a population and provide accurate estimates of annual influenza vaccine effectiveness (VE) to prevent medically-attended, influenza-associated illness in the population for whom influenza vaccination is recommended. Estimating influenza VE as soon as possible after the start of a seasonal influenza epidemic or pandemic, and monitoring it over time, are important to guide vaccination policies for influenza control. Estimation of VE depends upon accurate assessment of vaccination status, laboratory-confirmed disease outcomes, timing of illness and vaccination, and assessment of other factors that may affect vaccine use and immune response to vaccination. Moreover, a number of potential modifiers of vaccine response and vaccine effectiveness have been identified, including individual factors (age, prior vaccination), environmental factors (exposure to cigarette smoke), viral factors (influenza type and subtype) and infectious disease factors. This FOA intends to solicit applications that describe plans to identify and control for a variety of potential confounders in each proposed analysis. In addition, this network will allow comparison of VE data for specific vaccine types available in the US and serve as an emergency response resource in the event of an influenza pandemic. Results from research conducted under this funding opportunity announcement will yield high impact public health findings and/or strategies that will contribute to a reduction in the overall healthcare burden and improve the health of the US population. Participating institutions awarded

under this FOA will coordinate enrollment of patients aged 6 months and older with acute respiratory illness (ARI) and influenza infection will be confirmed using a standardized reverse-transcription PCR assay. Participating sites will contribute data to CDC to estimate VE using a test-negative study design. Applications should describe plans to identify and control for a variety of potential confounders in each proposed analysis. Annual VE estimates will be used to inform and assess the public health impact of influenza vaccination programs on the prevention of medically-attended, influenza-associated illness.

- **Mechanism of Support.** Cooperative Agreement
- **Funds Available and Anticipated Number of Awards.** The estimated total funding for the five-year project period is $30,000,000. The estimated total funding for the first budget period is $5,400,000. These fund estimates include the budgets for Core Components, Additional Components and Optional Components, which are described in Section II. The anticipated number of Core Component awards is up to five; Additional Component awards is up to five; Optional Component A awards is up to one; and Optional Component B awards is up to three. The awards issued under this FOA are contingent upon availability of funds, the total number of meritorious applications and the cost of the applications received. See Section II. “Award Information” for funding information by individual component and by year.
- **Budget and Project Period.** The project period will run from 07/01/2016 to 06/30/2021. The estimated average funding (direct and indirect) for the first budget period (7/01/2016 to 6/30/2017) will be up to $1,300,000 per awardee.
- **Application Research Strategy Length:** Page limits for the Research Strategy component of the Research Plan are clearly specified in Section IV "Application and Submission Information" of this funding opportunity 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 per application. If necessary, Co-PI(s) may be listed in the application but only one PI may be the primary CDC contact for the award and this must be indicated in the application.
- **Number of Applications.** Eligible applicant institutions may submit only one application containing multiple components. See Part 2. Section I.2 for further information.
- **Application Type.** New
- **Special Date(s).** A potential applicant conference call will be held on Thursday, December 3, 2015 at 12 noon ET. The bridge number is 1-866-662-8986, passcode 8378091.
- **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

Sections 317, 317(k)(2) of the Public Health Service Act (42 U.S.C. Sections 247b, 247b(k)(2) and 247c), as amended.

1. Background and Purpose

Influenza is an important cause of morbidity, mortality, and healthcare burden across all age groups. Because influenza viruses are constantly changing and vaccines are reformulated every year, annual estimates of the effectiveness of influenza vaccines in preventing influenza infection and its associated complications are needed in order to evaluate the protection provided by annual, nationwide vaccination programs. Each year in the United States, influenza viruses infect up to 20% of the population and cause hundreds of thousands to millions of medically-attended illnesses and thousands of hospitalizations and deaths. Annual influenza vaccination is the primary influenza prevention strategy and is recommended for all people ≥ 6 months of age in the U.S. Many studies have described the vaccine effectiveness (VE) of seasonal and 2009 pandemic influenza vaccine formulations against laboratory-confirmed symptomatic and medically-attended outpatient influenza illness (Griffin, 2011; Treanor, 2012; Ohmit, 2014; McLean 2014). In recent seasons, effectiveness of influenza vaccines has varied by influenza virus type and subtype or lineage, antigenic match between vaccine and circulating viruses, patient characteristics including age and prior vaccination history, and vaccine type. This FOA seeks to support a network of research institutions to estimate the annual effectiveness of influenza vaccination to prevent laboratory-confirmed, influenza-associated illness and to provide additional information on factors associated with influenza vaccine effectiveness.

The effectiveness of influenza vaccination varies yearly due to continual evolution of circulating virus strains and changes in annual influenza vaccine formulations. Thus, VE estimates from multiple seasons are necessary to estimate the public health impact of different licensed vaccine formulations used in national vaccination programs, including inactivated and live-attenuated vaccines, as well as high dose and standard dose inactivated vaccines currently available for older adults in the US. Observational studies of licensed vaccines add new information about vaccine effectiveness in “real world” populations, settings and age groups, not generally included in clinical trials. Comparable data from multiple years and from multiple sites are required to accurately assess and estimate VE against influenza virus A subtypes and B lineages and for different licensed vaccines.

Most current research to assess VE against influenza ambulatory visits uses a test-negative study design (Jackson, 2013; DeSerres, 2013; Foppa, 2013; Sullivan, 2014). Patients seeking care for acute respiratory illness (ARI) are recruited for study enrollment and systematically tested for influenza infection using sensitive molecular-based diagnostic assays (e.g., RT-PCR) (CDC, 2014). Influenza-positive patients are identified as study cases and influenza-negative patients as controls. The use of sensitive diagnostic testing for influenza reduces biases that can affect VE estimates (Orenstein, 2007; Ferdinands, 2012; Jackson, 2015). During the influenza season, influenza viruses are detected in 10-40% of persons with ARI who seek care in ambulatory care settings, depending upon the influenza season. Also, most patients presenting to ambulatory care for ARI present within 7 days of illness onset, a time when detecting influenza viruses is optimal.

References:

1) De Serres, G., *et al.* The test-negative design: validity, accuracy and precision of vaccine efficacy estimates compared to the gold standard of randomised placebo-controlled clinical trials. Euro Surveill, 2013. **18**(37).

2) Ferdinands, J.M. and D.K. Shay. Magnitude of potential biases in a simulated case-control study of the effectiveness of influenza vaccination. Clin Infect Dis, 2012. **54**(1): p. 25-32.

3) Foppa, I.M., *et al.* The case test-negative design for studies of the effectiveness of influenza vaccine. Vaccine, 2013. **31**(30): p. 3104-9.

4) Griffin, M.R., *et al.* Effectiveness of non-adjuvanted pandemic influenza A vaccines for preventing pandemic influenza acute respiratory illness visits in 4 U.S. communities. PLoS One, 2011. **6**(8): p. e23085.

5) Jackson, M.L. and J.C. Nelson. The test-negative design for estimating influenza vaccine effectiveness. Vaccine, 2013. **31**(17): p. 2165-8.

6) Jackson, M.L. and K.J. Rothman. Effects of imperfect test sensitivity and specificity on observational studies of influenza vaccine effectiveness. Vaccine, 2015. **33**(11): p. 1313-6.

7) McLean, H.Q., *et al.* Influenza vaccine effectiveness in the United States during 2012-2013: variable protection by age and virus type. J Infect Dis, 2015. **211**(10): p. 1529-40.

8) Ohmit, S.E., *et al*. Influenza vaccine effectiveness in the 2011-2012 season: protection against each circulating virus and the effect of prior vaccination on estimates. Clin Infect Dis, 2014. **58**(3): p. 319-27.

9) Orenstein, E.W., *et al.* Methodologic issues regarding the use of three observational study designs to assess influenza vaccine effectiveness. Int J Epidemiol, 2007. **36**(3): p. 623-31.

10) Sullivan, S.G., S. Feng, and B.J. Cowling. Potential of the test-negative design for measuring influenza vaccine effectiveness: a systematic review. Expert Rev Vaccines, 2014. **13**(12): p. 1571-91.

11) Treanor, J.J., *et al.* Effectiveness of seasonal influenza vaccines in the United States during a season with circulation of all three vaccine strains. Clin Infect Dis, 2012. **55**(7): p. 951-9.

Healthy People 2020 and other National Strategic Priorities

The CDC NCIRD within HHS is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2020" (http://www.healthypeople.gov/2020/topicsobjectives2020/default) and to measuring program performance as stipulated by the Government Performance and Review Act (GPRA). This FOA is in alignment with the "Healthy People 2020" priority focus area, Immunization and Infectious Diseases and HHS Strategic Plan Goals and Objectives: Goal 3 - Advance the Health, Safety, and Well-Being of the American People: http://www.hhs.gov/about/strategic-plan/strategic-goal-3/index.html

Public Health Impact

Annual VE estimates will be used to inform and assess the public health impact of influenza vaccination programs on the prevention of medically-attended, influenza-associated illness. In addition, this network will allow comparison of VE data for specific vaccine types available in the US and serve as an emergency response resource in the event of an influenza pandemic. Results from research conducted under this FOA will yield high impact public health findings and/or strategies that should contribute to a reduction in the overall healthcare burden and improve the health of the US population.

Relevant Work

1) FOA (IP-11-003): Annual Estimates of Influenza Vaccine Effectiveness for Preventing Laboratory-Confirmed Influenza in the United States (http://www.grants.gov/web/grants/search-grants.html , Keyword: RFA-IP-11-003; Opportunity Status: Archived)

2) Guidance for Clinicians on the Use of RT-PCR and Other Molecular Assays for Diagnosis of Influenza Virus Infection at http://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm

3) Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2015–16 Influenza Season, MMWR http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6430a3.htm

2. Approach

Objectives/Outcomes

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

Each application MUST address the Core Component and the two Additional Components. In addition, applications may address up to two Optional Components, but no more than one will be awarded to the same applicant.

A. Core Component (Mandatory) for Years 1-5, $800,000 per year (direct and indirect costs):

Assess influenza vaccine effectiveness (VE) in preventing laboratory-confirmed influenza infections among children and adults with medically-attended, acute respiratory illness (MAARI) who present for care in ambulatory settings. The application should address all of the following objectives:

1) Describe research study activities and operations as outlined below. Applications must include, at a minimum, details of study activities to:

a) Document study resources, capabilities and proposed activities to achieve acceptable study sample size enrollments using conservative assumptions of influenza activity during a typical influenza season (e.g., at least 1000 total enrollees with a minimum of 300 in each of three age groups [6 months – 17 years, 18-49 years and 50 years and older], with at least 100 among young children aged 6 months – 8 years and with at least 100 among adults aged ≥65 years);

b) Describe procedures for enrollment of ambulatory patients in a research study at participating health facilities. Describe possible approaches to increase proportion of enrollment (up to 25% of total enrollment) from priority groups, such as children aged 6 months to 8 years and adults aged 65 years and older;

c) Describe procedures for collection of research specimens from all enrolled patients;

d) Describe study patient identification and enrollment protocols to achieve a goal of >60% participation among eligible participants. Describe methods to identify and correct possible problems with study enrollment, including participation of <50% of eligible persons and failure to meet sample size;

e) Obtain detailed patient data from enrolled patients including information on age, co-morbidities and vaccination history for current and prior seasons;

f) Describe methods for validation of vaccination status with medical records, state immunization registries and records from vaccine providers.

2) Describe how patients with ARI will be identified and enrolled during each influenza season covered by the five-year project period. Provide diagrams and/or algorithms demonstrating how patients will be screened for eligibility and describe the participant enrollment forms that will be used to monitor study participation.

a) Provide a detailed description of each participating facility where patients will be enrolled and who will perform the enrollment. Include information for each performance site that indicates compliance with human subjects research protections, including Federal-Wide Assurance numbers (FWAs). Institutions that will establish a reliance on an external organization's FWA or Institutional Review Board (IRB) should provide information on the appropriate authority for that organization and provide a statement of intent to establish a written agreement between the study institution and the other institution/organization, outlining adherence to requirements of the U.S. Federal Policy for the Protection of Human Subjects. Describe facility policies on patient enrollment in clinical research (e.g., do research staff need to request provider permission before the patient is approached by research staff or do clinical staff need to ask patient permission to have research staff approach patient?). If a clinician step is required at the institution, describe how the site will remove this potentially biasing barrier for this study.

b) Describe proposed partnerships and the methods of local surveillance that will be used to identify the start and end of the influenza season and, therefore, define the specific study enrollment and testing period

for their sites.

c) Descriptions of previous experience enrolling patients in research studies conducted in ambulatory settings are useful and encouraged, including strategies to achieve a high rate of participation among approached patients and information from previous studies comparing target enrollment to actual number enrolled.

3) Describe how the following proposed total study sample enrollment populations will be achieved.

a) For each influenza season: Enrollment of a minimum of 1000 ambulatory patients presenting with ARI and cough within 7 days of illness onset.

For planning purposes, the following conservative assumptions were used to estimate sample size populations:

- Influenza detection in 14% of patients with ARI meeting inclusion criteria;
- VE estimate = 50%;
- Vaccine coverage = 50%, with 10% of enrollees with indeterminate vaccination status;
- Five network sites, three strata for analysis (e.g., age group, influenza virus type/subtype-specific VE);
- Alpha=0.05, Power= 0.80.

Overall, each applicant institution will need to demonstrate the capacity or history to enroll a minimum of 1000 ARI patients per season (this FOA foresees 5000 total for all five awardees to identify a total of 700 influenza-positive cases) to estimate an overall influenza A and B VE each year by age group or VE by influenza virus type/subtype for all ages, depending upon the frequency and distribution of influenza virus types and subtypes. It is expected that during seasons of increased influenza circulation, higher numbers of influenza-positive cases would be enrolled, providing additional age-group specific, vaccine-specific and influenza subtype-specific VE estimates.

4) Diagnose influenza cases by virus type and subtype or lineage using a standardized, validated real-time RT-PCR assay (with probes, primers and reagents approved by CDC). The application should:

a) Provide evidence of competency in the use of the RT-PCR assay or evidence that the contracting laboratory performing the testing has expertise with the RT-PCR assay (e.g., number of these assays run/year; comparisons to other assays or results from validation studies, other measures of proficiency; letters of support; and publications);

b) Provide a statement of agreement to participate in CDC-sponsored proficiency testing throughout the term of the project. Proficiency testing may include testing a small panel of specimens sent by CDC and reporting results back to CDC within a specified timeframe (generally, 1 month);

c) Describe experience to aliquot specimens and prepare shipments of aliquots (0.5-1.0 ml) for antigenic characterization, sequencing, special research studies and for other WHO Influenza Collaborating Center surveillance purposes performed at CDC and contract laboratories or similar research. For planning purposes, assume specimen shipments will be required every 2 to 4 weeks during the influenza season and will require accompaniment of a completed WHO surveillance form (supplied by CDC). Include a description of how respiratory specimens will be stored and whether leftover specimen aliquots will be available.

5) Describe methods to obtain current season influenza vaccination status (including vaccination date(s), vaccine type, and manufacturer) and prior season vaccination status (including vaccination type) using self-report and verification from electronic medical records, real-time electronic vaccine registries or medical abstraction from health care providers, pharmacy chains, schools, and other potential vaccine providers. The application should describe procedures for verification of self-reported vaccination status, including procedures to obtain documentation of vaccination from providers not captured by electronic medical records or immunization registries.

a) Include vaccination information that will be collected from each study participant/enrollee (e.g., date of vaccination for current season vaccination and vaccine provider, receipt of influenza vaccine in prior seasons);

b) Evidence of experience and competence with methods to verify influenza vaccination status is helpful;

c) Describe recent evaluations of self-reported and record/registry-based vaccination status (validation of vaccine verification methods) or describe methods that will be used to evaluate vaccine verification in the first year of the project.

6) Describe methods to collect information from enrolled patients about onset of illness, symptoms, self-reported health status, self-reported illness severity and household characteristics (including number of occupants and cigarette smoking) by patient interview. Describe methods to collect additional information to investigate differences in healthcare utilization among vaccinated and unvaccinated individuals (such as number of outpatient visits for any reason in the preceding 12 month period), and the local practice norms of the medical settings and their health care providers (including any diagnostic testing for influenza).

7) Describe methods to collect post-enrollment information on date of resolution of symptoms, date of return to normal activities and impact of illness on daily activities by electronic survey or telephone interview.

8) Describe methods to collect information from enrolled patients about high-risk medical conditions of influenza, antiviral and antibiotic use (date and drugs), complications of illness (hospitalization, subsequent medical encounters and procedures during the 30-day period following enrollment) and diagnostic codes associated with medical encounters (ICD-9 or ICD-10 codes) (ICD: International Classification of Diseases) using electronic medical records.

9) Describe a plan to:

a) Provide periodic updates (every 2 weeks) on enrollment of cases and controls, RT-PCR results and status of data collection; and

b) Provide data to CDC for interim (mid-season) and end-of-season VE estimates according to established timelines, normally 4-6 weeks after the beginning of enrollment for interim estimates.

10) Propose methods to provide annual estimates of population-based incidence of medically-attended, laboratory-confirmed influenza in ambulatory settings using data from a source population for health facilities where enrollment takes place. Describe a plan to provide incidence data to CDC for annual estimates of influenza-related disease burden.

11) Provide a statement on the research capacity and willingness to serve as an emergency response resource and participate with CDC in pandemic-related studies related to vaccine and antiviral assessments and estimation of incidence outside of normal seasonal study activities, should they be needed.

B. Two Additional Components (Mandatory) for Years 3-5 at $100,000 each, thus $200,000 total per year (direct and indirect costs):

1) Evaluation of disease burden due to respiratory syncytial virus (RSV) and other respiratory viruses during the influenza season

New vaccines are currently under development for RSV. Determining the burden of RSV before and after vaccine introduction would help to evaluate the impact of the new vaccine. If there is a potential for RSV vaccines to become available in the near future, a goal would be to directly measure VE for the new vaccine against medically-attended illness in this network. Sites should be willing to test for RSV and other respiratory viruses using CDC-approved assays (CDC may provide probes, primers and reagents, if applicable). In addition, sites should contribute to multi-site evaluations comparing influenza test-positive patients to patients who test positive for other respiratory viruses to examine effects of influenza vaccination

on illness due to other respiratory viruses. All applications should provide responses for the following:

a) Describe the current capability and diagnostic test methods available for the detection of RSV and other respiratory viruses (molecular assays are preferred);

b) Describe the methods that would be used to estimate the population-based incidence of medically-attended illness associated with laboratory-confirmed infection with RSV and other respiratory viruses among adults (18-64), older adults (≥65 years), and children (under 18). For this study, disease burden among children <6 months of age will not be determined;

c) Describe the methods that would be used to obtain RSV vaccination data, should RSV vaccines become available.

2) Pandemic Preparedness

In the event of an influenza pandemic, participating sites would be involved in pandemic response activities, including studies to describe the epidemiology of novel influenza virus infection and burden of disease, and to evaluate use and effectiveness of antiviral agents for treatment and effectiveness of seasonal and pandemic influenza vaccines for prevention of pandemic influenza. All applications should provide responses for the following:

a) Capacity to participate with CDC in pandemic-related studies during or outside of the normal seasonal study activities, modify protocol to align with protocols for pandemic-related studies and prepare operational plans for implementation of pandemic studies

b) Willingness to pilot methods that might be needed to conduct pandemic-related studies. For example, identification and collection of respiratory specimens from ill persons triaged by telephone; or collection of post-antiviral treatment specimens from influenza-positive individuals to evaluate for the emergence of antiviral resistance during treatment (tested at a CDC laboratory).

C. Two Optional Components (A and B)

Each applicant may apply for up to two of the Optional Components listed below for Years 1-5; only one Optional Component (A or B) will be funded per applicant and only if the mandatory Core Component is awarded to that applicant.

1) Optional Component A: Evaluation of the development of antibody profiles over multiple influenza seasons in a household cohort (up to $500,000 per year including direct and indirect costs).

Identify and enroll a minimum of 400 households, including young children aged 3 years or younger, to conduct active surveillance for acute respiratory infection among young children and their household members over multiple influenza seasons and to collect serum specimens twice yearly from household members and a subset of children aged <3 years to study the development of antibodies to influenza viruses in young children. Applications should present a strategy to identify and enroll a longitudinal cohort of at least 180 children aged <3 years (n=60 aged <1 year, n=60 aged 1-2 years and n=60 aged 2-3 years) to be followed over two to five influenza seasons, including pre- and post-season serum specimen collection; collect, process and store serum specimens before and at the end of the influenza season, as well as 4 weeks after influenza vaccination (if applicable); propose a method to collect respiratory specimens from symptomatic young children and their household members within 7 days of illness onset. Applications should present a comprehensive strategy for enrolling households of families including infants and young children, optimizing response rates, and minimizing attrition. The applications should plan to estimate the incidence of laboratory-confirmed influenza infection (of any severity) among young children and household members, estimate vaccine effectiveness and compare these with estimates of VE against medically-attended influenza illness. The application should describe the investigators' willingness to send serum specimens for

investigation by CDC's influenza laboratory to understand effects of natural infection and vaccination on immune responses to reference influenza viruses for the development of antibody profiles. CDC will test paired sera by hemagglutination-inhibition assay methods by a single reference laboratory using standard, validated procedures.

2) Optional Component B: Immunologic study of response to influenza vaccination (up to $300,000 per year including direct and indirect costs).

Recruit and enroll 150 to 200 subjects in priority age groups (6 months-8 years, and adults 65 and older) who are eligible to receive specific influenza vaccines and for whom the vaccines are recommended to study the immune responses to influenza vaccines. The application should describe the vaccination strategy and how the investigators will collect, process, store, and ship paired serum specimens to a reference laboratory designated by CDC. The application should describe the investigators' willingness to participate in cross-site decisions on specific influenza vaccines and populations to be examined (for example, live-attenuated vaccine in children and adolescents or high dose inactivated vaccine in persons aged ≥65 years) and interpretation of influenza vaccine response.

Applications should:

a) Describe a process to enroll 150 to 200 subjects for collection of serum specimens on or before the date of vaccination and 4 weeks after receipt of vaccine. Specimens will be processed and shipped to the CDC or designated laboratory for influenza testing. The CDC will be responsible for testing paired sera by hemagglutination-inhibition assay methods by a single reference laboratory using standard, validated procedures.

b) Identify priority groups for investigation of cell-mediated immune responses; describe experience or provide evidence that the contracting laboratory has experience with collection, processing and storage of peripheral blood mononuclear cells (PBMC), including measures of cell count and viability; provide letters of support or publications. The CDC will be responsible for testing these specimens.

c) Describe how participants will be enrolled and followed during the study period, including steps to minimize and measure potential selection and attrition biases.

d) Describe how prior vaccination and laboratory-confirmed influenza infection, other medical and health information about the participants gathered from interview, medical record extraction, or chart abstraction can be used to examine the potential modifiers of vaccine response.

Target Population

Mandatory components: Children (from 6 months of age) and adult (≥18 years) populations presenting to ambulatory facilities with acute respiratory illness.

Optional components: Healthy children (from 6 months of age) and adult (≥18 years) individuals who agree to enroll in the household or vaccine response studies.

Collaboration/Partnerships

This FOA seeks to support a network of US institutions that can obtain reliable vaccination information for a population and provide accurate estimates of annual influenza vaccine effectiveness (VE) to prevent medically-attended, influenza-associated illness in the population for whom influenza vaccination is recommended. The awardees will work cooperatively with CDC and other network site partners to collectively enroll sufficient numbers of the target population to provide interim and end-of-season VE estimates for population subgroups and factors of interest. Investigators from each site and CDC investigators will participate on a steering committee.

Evaluation/Performance Measurement

As part of the application, the PI should include measurable goals and aims based on a five-year research project period. The grantee 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. Also, funded PIs must submit an annual progress report showing their activities and outcomes based on their overall research goals and timeline. For more information on required Reporting, please see Section VI of this FOA.

For all components, the application should include an evaluation/performance measurement plan. Progress should be identified by achievement of relevant milestones which may include, but not limited to:

- The type of evaluations (i.e., process, outcome or both) to be conducted.
- Key evaluation questions.
- Other information (e.g., performance measures to be developed by the applicant).
- Potentially available data sources and feasibility of collecting appropriate evaluation and performance data.

Translation Plan

For all components, the application should describe how the findings of this work will inform and evaluate influenza vaccine policy and recommendations, including providing annual estimates of influenza vaccine effectiveness against circulating influenza viruses. 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. Describe how the findings could be generalized and scaled to populations and communities outside of the funded project.

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: $30,000,000

Applicants MUST apply for the mandatory Core Component (Years 1-5) and the mandatory two Additional Components (Years 3-5). Applicants may also apply for Optional Component A and Optional Component B (Years 1-5), but only one Optional Component (A or B) will be awarded to an applicant who has been awarded the Mandatory Components (Core and two Additional Components). Awards issued under this FOA are contingent on the availability of funds and submission of a sufficient number of meritorious applications.

Estimated funds available for Mandatory Components (Core plus two Additional Components) per awardee per year:

Year 1: $800,000

Year 2: $800,000

Year 3: $1,000,000

Year 4: $1,000,000

Year 5: $1,000,000

Anticipated Number of Awards for Mandatory Components (Core plus two Additional Components): Up to five awards

Estimated funds available for Optional Component A is $500,000 per award per year.

Estimated funds available for Optional Component B is $300,000 per award per year.

Anticipated Number of Awards for Optional Components: 1 Optional Component A and up to 3 Optional Component B awards.

Estimated total funding available for first year:

$5,400,000: 5 sites x $800,000 (Core + Additional Components) + 1 x $500,000 Optional Component A + 3 x $300,000 Optional Component B.

Estimated total funding available for entire project period: $30,000,000 ($5,400,000 for each of Years 1 and 2 + $6,400,000 for each of Years 3, 4, and 5)

Anticipated Number of Awards: 5

Ceiling for the Core + Additional Components per awardee per year: $1,000,000.

Floor for the Core + Additional Components per awardee per year: $500,000.

Ceiling for Optional Component A per award per year: $500,000

Floor for Optional Component A per award per year: $200,000.

Ceiling for Optional Component B per award per year: $300,000

Floor for Optional Component B per award per year: $100,000.

The award ceiling and floor and total project period listed below are for the Core + Additional Components.

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

Award Ceiling:	$1,000,000 Per Project Period
Award Floor:	$500,000 Per Project 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:

State governments
County governments
City or township governments
Special district governments
Independent school districts
Public and State controlled institutions of higher education
Native American tribal governments (Federally recognized)
Public housing authorities/Indian housing authorities
Native American tribal organizations (other than Federally recognized tribal governments)
Nonprofits having a 501(c)(3) status with the IRS, other than institutions of higher education
Nonprofits without 501(c)(3) status with the IRS, other than institutions of higher education
Private institutions of higher education
Others (see text field entitled "Additional Information on Eligibility" for clarification)

Additional Eligibility Category:

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

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

Nonprofits Other Than Institutions of Higher Education:

Nonprofits (Other than Institutions of Higher Education)

Governments:

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

Other:

Native American tribal organizations (other than Federally recognized tribal governments)
Faith-based or Community-based Organizations
Regional Organizations

Foreign Organizations: a Foreign Organization is a public or private organization, whether non-profit or for-profit, located in a country other than the United States (U.S.) and its territories that is subject to the laws of the country in which it is located, irrespective of the citizenship of project staff or place of performance.
Bona Fide Agents: a Bona Fide Agent is an agency/organization identified by the state as eligible to submit an application under the state eligibility in lieu of a state application. If applying as a bona fide agent of a state or local government, a legal, binding agreement from the state or local government as documentation of the status is required. Attach with "Other Attachment Forms" when submitting via www.grants.gov.
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 http:// ecfr.gpoaccess.gov /cgi/t/text/ text-idx?c=ecfr& sid=512ff78311f427c00454772dcf21523a&rgn=div8 &view=text&node=48:1.0.1.6.34.0.1.18& idno=48

2. Foreign Organizations

Foreign Organizations are not eligible to apply.

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

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

3. Special Eligibility Requirements

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

If a current awardee of CDC FOA IP11-003 applies to this FOA and the application ranks sufficiently high to be awarded, funding restrictions will apply to ensure no overlap of the budget or project periods with IP11-003 and IP16-002.

4. Justification for Less than Maximum Competition

N/A

5. Responsiveness

If the investigators plan to use their State Health Department laboratory or contract laboratory services for RT-PCR and viral cultures, then documents supporting this partnership must be submitted.

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 institution (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 (TIMS) staff at (770) 488-2700 or pgotim@cdc.gov for further instructions. Hours: Monday - Friday, 7am – 4:30pm U.S. Eastern Time. CDC Telecommunications for the hearing impaired or disabled is available at: TTY 1-888-232-6348.

2. Content and Form of Application Submission

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

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

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

3. Letter of Intent

Due Date for Letter of Intent: **12/14/2015**

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

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

Name of the Applicant

Descriptive title of proposed research

Name, address, and telephone number of the PD(s)/PI(s)

Names of other key personnel

Participating institutions

Number and title of this funding opportunity

The letter of intent should be sent to:

Gregory Anderson, MPH, MS

Extramural Research Program Office

Office of the Associate Director of Science

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

Centers for Disease Control and Prevention

U.S. Department of Health and Human Services

1600 Clifton Road, MS E-60

Atlanta, GA 30333

Telephone: 404-718-8833

Fax: 404-718-8822

Email: GAnderson@cdc.gov

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 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)

Your application is subject to Intergovernmental Review of Federal Programs, as governed by Executive Order 12372 (http://www.archives.gov/federal-register/codification/executive-order/12372.html). This order sets up a system for state and local review of proposed federal assistance applications. You should contact your state single point of contact (SPOC) as early as possible to alert the SPOC to prospective applications, and to receive instructions on your state's process. Click on the following link to get the current SPOC list: http://www.whitehouse.gov/omb/grants_spoc/.

11. Funding Restrictions

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.

The Paperwork Reduction Act of 1995 (PRA): Applicants should be advised that any activities involving information collection (i.e., posing similar questions or requirements via surveys, questionnaires, telephonic requests, focus groups, etc.) from 10 or more non-Federal entities/persons, including States, are subject to PRA requirements and may require CDC to coordinate an Office of Management and Budget (OMB) Information Collection Request clearance prior to the start of information collection activities. This would also include information sent to or obtained by CDC via forms, applications, reports, information systems, and any other means for requesting information from 10 or more persons; asking or requiring 10 or more entities/persons to keep or retain records; or asking or requiring 10 or more entities/persons to disclose information to a third-party or the general public.

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 US 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.

If a current awardee of CDC FOA IP11-003 applies to this FOA and the application ranks sufficiently high to be awarded, funding restrictions will apply to ensure no overlap of the budget or project periods with IP11-003 and IP16-002.

12. Other Submission Requirements and Information

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

Important reminders: All PD/PIs must include their eRA Commons ID in the Credential field of the

Senior/Key Person Profile Component of the SF 424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to CDC.
The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management (SAM). Additional information may be found in the SF424 (R&R) Application Guide.
If the applicant has an FWA number, enter the 8-digit number. Do not enter the letters "FWA" before the number. If a Project/Performance Site is engaged in research involving human subjects, the applicant organization is responsible for ensuring that the Project/Performance Site operates under and appropriate Federal Wide Assurance for the protection of human subjects and complies with 45 CFR Part 46 and other CDC human subject related policies described in Part II of the SF 424 (R&R) Application Guide and in the HHS Grants Policy Statement.
See more resources to avoid common errors and submitting, tracking, and viewing applications: http:// grants.nih. gov/grants/ Electronic Receipt /avoiding_ errors.htm or http:// grants. nih.gov/grants/ Electronic Receipt/submit_ app.htm
Upon receipt, applications will be evaluated for completeness by the CDC Office of Grants Services (OGS) and responsiveness by OGS and the Center, Institute or Office of the CDC. Applications that are incomplete and/or nonresponsive will not be reviewed.

Section V. Application Review Information

1. Criteria

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

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

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

Significance

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

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?

Do the investigators have the appropriate training and skills to conduct this study? Do the members of the investigative team demonstrate experience conducting assessment in ambulatory settings, as documented in their biosketches and/or by publications in peer-reviewed journals? Do the investigators have experience verifying vaccination dates, as well as vaccine type and product information among enrollees from ambulatory settings? Do the investigators demonstrate epidemiologic, behavioral, clinical, administrative, and management experience needed to conduct the proposed study? Does the investigative team bring complementary and integrated expertise to the project (if applicable)? Do the investigators have the ability to collect, manage, and analyze accurate data in a timely manner? Does the application identify access to qualified personnel with realistic and sufficient percentage-time commitments to achieve the objectives identified in each phase of the study?

For Optional Component A only:

Do the investigators have experience recruiting and enrolling households including both adult members and young children for participation in longitudinal studies? Do the investigators have experience collecting blood from study participants, especially young children, in community settings? Do the investigators have experience conducting active surveillance for acute respiratory illness among enrolled study participants during an influenza season, and collecting specimens from symptomatic individuals to test for influenza and other respiratory viruses?

For Optional Component B only:

Do the investigators have experience recruiting and enrolling individuals for participation in studies examining immune response to vaccination involving collection of blood specimens, including peripheral blood mononuclear cells (PBMCs), from enrolled study participants before and after vaccination?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Does the application demonstrate an understanding of the relevant theoretical, empirical, and methodological issues relevant to the study?

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?

Does the application include research study plans that address each of the identified objectives stated in Part 2. Section I.2 Approach? Does the application include a mix of insurance types, including private and public options? Does the application clearly demonstrate the potential to enroll an adequate sample size?

Does the application describe how the applicant will work with collaborating clinics to gain access to sufficient numbers of the selected target population and achieve the testing frequencies identified to successfully conduct the proposed study?

For Additional Components Only:

Does the application describe capability and proposed methods to evaluate disease burden due to RSV and other respiratory viruses during the influenza season?

Does the application describe capacity to participate in pandemic-related studies and pilot methods that might be needed to conduct pandemic-related studies?

For Optional Component A only:

Does the application describe methods to recruit and retain enrolled households for the duration of an influenza season and over multiple seasons? Does the application describe the approach to identify, collect specimens from and interview study participants with influenza-related symptoms who do not seek care for their illness?

For Optional Component B only:

Does the application clearly demonstrate the potential to enroll 150-200 individuals from priority age groups (either young children aged 6 months – 8 years or older adults aged 65 years and older)? Does the application describe how prior vaccination, history of laboratory-confirmed influenza infection, medical history and health information will be assessed among enrolled study participants?

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?

Do applicant institutions perform or demonstrate partnerships with laboratories (e.g., state public health, research, contract laboratories) that utilize pre-existing molecular (nucleic acid-based) testing protocols with a high sensitivity similar to RT-PCR for the detection of influenza A virus (including H3N2 and H1N1 subtypes and influenza B), and are able to demonstrate a high level of study testing capability (e.g., testing for research purposes only) during the duration of the influenza season (~12 weeks)(See Part 2.Section I.2 Research)?

Will the planned location for the study provide access to adequate numbers of the proposed target population? Do the applicant or collaborating clinics indicate their agreement to participate to achieve the study objectives throughout the duration of the project period of award? Does the application provide a description of procedures for management of data security and participant confidentiality in order to achieve the research objectives? Are applicant institutions associated with organizations that provide primary care services including immunizations to large, diverse populations with both private and public healthcare insurance? Are applicant institutions associated with healthcare systems in which ambulatory clinics and immunization services are linked by an electronic medical records system?

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/grants/additionalrequirements/index.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 (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.

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/dual-use/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.

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 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 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.

For this FOA, the Mandatory Components (Core and Additional Components) will be scored together as a single application and rank ordered to determine awarding of funds. Selection of applications deemed to have the highest scientific and technical merit (streamlining) will be based on the Overall Impact Score for the Mandatory Components. Optional Components A and B will be scored separately from the Mandatory Components and from each other and rank ordered. Funding for the Optional Components will be limited to those applications recommended for funding of the Mandatory Components.

Funds will be awarded to the top ranked Optional Component A and three top ranked Optional Component B projects. If one application has two Optional Components ranked as the top scoring Optional Components A and B, this application will be awarded Optional Component A. If scores for any of the Optional Components are tied, the applications with the top ranking Mandatory Components will be awarded the Optional Component, with Optional Component A being awarded first and then Optional Component B.

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 75, 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-7: Executive Order 12372 Review

AR-9: Paperwork Reduction Act Requirements

AR-10: Smoke-Free Workplace Requirements

AR-11: Healthy People 2020

AR-12: Lobbying Restrictions

AR-13: Prohibition on Use of CDC Funds for Certain Gun Control Activities

AR-14: Accounting System Requirements

AR-16: Security Clearance Requirement

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

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

AR-22: Research Integrity

AR-24: Health Insurance Portability and Accountability Act Requirements

AR-25: Release and Sharing of Data

AR-26: National Historic Preservation Act of 1966

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

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

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

AR 31 - Distinguishing Public Health Research and Public Health 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.

The following are 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/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.

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/obesity/strategies/food-serv-guide.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.

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

Copyright Interests Provision This provision is intended to ensure that the public has access to the results and accomplishments of public health activities funded by CDC. Pursuant to applicable grant regulations and CDC's Public Access Policy, Recipient agrees to submit into the National Institutes of Health (NIH) Manuscript Submission (NIHMS) system an electronic version of the final, peer-reviewed manuscript of any such work developed under this award upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. Also at the time of submission, Recipient and/or the Recipient's submitting author must specify the date the final manuscript will be publicly accessible through PubMed Central (PMC). Recipient and/or Recipient's submitting author must also post the manuscript through PMC within twelve (12) months of the publisher's official date of final publication; however the author is strongly encouraged to make the subject manuscript available as soon as possible. The recipient must obtain prior approval from the CDC for any exception to this provision.
The author's final, peer-reviewed manuscript is defined as the final version accepted for journal publication, and includes all modifications from the publishing peer review process, and all graphics and supplemental material associated with the article. Recipient and its submitting authors working under this award are responsible for ensuring that any publishing or copyright agreements concerning submitted articles reserve adequate right to fully comply with this provision and the license reserved by CDC. The manuscript will be hosted in both PMC and the CDC Stacks institutional repository system. In progress reports for this award, recipient must identify publications subject to the CDC Public Access Policy by using the applicable NIHMS identification number for up to three (3) months after the publication date and the PubMed Central identification number (PMCID) thereafter.

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

Dual Use Research of Concern On September 24, 2014, the US Government Policy for the Institutional Oversight of Life Sciences Dual Use Research of Concern was released. Grantees (foreign and domestic) receiving CDC funding on or after September 24, 2015 are subject to this policy. Research funded by CDC involving the agents or toxins named in the policy, must be reviewed to determine if it involves one or more of the listed experimental effects and if so, whether it meets the definition of DURC. This review must be completed by an Institutional Review Entity (IRE) identified by the funded institution.
Recipients also must establish an Institutional Contact for Dual Use Research (ICDUR). The award recipient must maintain records of institutional DURC reviews and completed risk mitigation plans for the term of the research grant, cooperative agreement or contract plus three years after its completion, but no less than eight years, unless a shorter period is required by law or regulation.
If a project is determined to be DURC, a risk/benefit analysis must be completed. CDC will work collaboratively with the award recipient to develop a risk mitigation plan that the CDC must approve. The USG policy can be found at http://www.phe.gov/s3/dualuse.
Non-compliance with this Policy may result in suspension, limitation, restriction or termination of USG funding, or loss of future USG funding opportunities for the non-compliant USG-funded research project and of USG funds for other life sciences research at the institution, consistent with existing regulations and policies governing USG funded research, and may subject the institution to other potential penalties under applicable laws and regulations.

4. Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and CDC grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial CDC programmatic involvement with the 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:

- Working with CDC scientists and other funded awardees to create a common protocol and research methods across sites, including:
    - Establishing common methods, measures, and procedures;
    - Establishing common recruitment and enrollment criteria;
    - Collecting and managing data in a format standardized across sites and compatible with other funded grantees (Note: this FOA will not support statistical assistance/analysis for individual sites as CDC program will provide it);
    - Establishing a common data dictionary and data management system;
    - Working with CDC scientists to refine protocols in order to improve the science based on reviewers' comments in the summary statement.
- Providing scientific and management oversight for the overall project at his/her performance site(s), including research design and conduct, data collection, quality control, data analysis and interpretation, and personnel management and serving on the Steering Committee.
- Obtaining and maintaining the appropriate Institutional Review Board approvals for all institutions or individuals participating in the research project, and working with CDC project scientists to obtain

Institutional Review Board approvals as required when CDC is engaged in research involving human subjects.

- Performing laboratory tests and data analyses as specified in the study protocols reviewed and approved by CDC.
- Participating in CDC-sponsored laboratory proficiency testing.
- Participating in network level coordination, research, and information dissemination across sites, including:
    - Agreeing to collaborate and share data with other awardees and CDC;
    - Participating in conference calls with project scientists to collaborate on the development of the research protocols and providing progress updates;
    - Describing research findings at regular intervals in project reports, and publishing the results in the peer-reviewed literature with CDC collaborators, as appropriate;
    - Completing bi-weekly updates on enrollment of cases and controls, laboratory test outcomes, and confirmed vaccination status;
    - Completing both mid-season and end-of-season delivery of data;
    - Budgeting travel expenses in the application so that investigators and personnel responsible for site coordination and data management are able to attend annual investigator meetings.
- Developing proposals for approval by the Steering Committee and leading secondary multi-site research projects, as well as conducting site-specific analyses to disseminate research findings.
- Establishing valid and reliable operations with laboratory where testing will be conducted, including the completion of proficiency panels to ensure the validity and reliability of PCR tests.
- Making the influenza-positive specimens detected during the study available to CDC for detailed antigenic and other laboratory analyses (e.g., antiviral resistance testing). The results of these analyses may be used for national and international decisions regarding the selection of influenza vaccine strains for subsequent influenza seasons. Original clinical material from a sample of influenza positive and influenza negative specimens must be made available to CDC for further testing. Viruses isolated from original clinical material may be considered for use as candidate vaccine seed strains.
- Recipient Organization will retain custody of and have primary rights to the information, data and software developed under this award, subject to U.S. Government rights of access consistent with current HHS/CDC policies.
- 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 Institutional Review Board approvals for all institutions or individuals engaged in the conduct of the research project.
- Working with CDC scientists to obtain OMB-PRA approvals, as needed.
- PUBLICATIONS/PRESENTATIONS: Publications, journal articles, presentations, 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 CDC Program abstracts or manuscripts prior to any publication related to this funding. The grantee will not seek to publish or present results or findings from this project without prior clearance and approval from CDC.
- 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).

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

- Advising on the development and implementation of a common protocol across sites for the evaluation influenza vaccine effectiveness.
- Providing definitions for acute respiratory infection (ARI), duration of influenza illness, and influenza

illness severity among children and adults.
- Providing a framework for evaluating possible confounders and modifiers of vaccine effectiveness including age, high-risk medical conditions, prior vaccination, and socio-demographic factors;
- Providing probes, primers, and reagents for RT-PCR testing (at minimum during the first year of the award and possibly during subsequent years) and guidelines for conducting laboratory tests;
- Providing a proficiency panel to be used in quality assurance for laboratory testing and be available to conduct additional tests on indeterminate lab results.
- Providing a framework and methods for recording and verifying vaccination status, vaccine type and manufacturer, and vaccination history.
- Providing a framework and methods for electronic medical record and medical chart abstraction.
- Maintaining custody of combined datasets and providing access to combined datasets for multisite analyses.
- Conducting data-management, data integration, statistical analysis, and reporting issues.
- Performing data analysis for primary vaccine effectiveness analyses and for other analyses, with input from participating site PIs.
- Preparing and leading multisite manuscripts of primary objectives (interim and end-of-season VE estimates and annual burden of disease estimates), as warranted.
- Working with grantees to develop a common set of evaluation tools and measures across sites.
- Working with grantees to develop an integrated data management system to be used across sites.
- Conducting sample size estimates for assessments of vaccine effectiveness for each grantee individually, and for all grantees combined.
- Conducting and coordinating serologic testing, analysis of serologic data and preparation of multisite manuscripts for serologic studies (optional components).
- Preparing the paperwork necessary for submission of research protocols to the CDC Institutional Review Board for review, as needed.
- Obtaining Office of Management and Budget approval per the Paperwork Reduction Act, if necessary.
- Assisting 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:

- Attending investigator meetings and participating in conference calls for the purposes of assessing overall progress, problem solving, and for program evaluation purposes.
- Collaborating on presentation and publication of data.
- Participating in Steering Committee activities to discuss new projects, authorship, and the resolution of conflicts.
- Collaborating 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, if needed.

Additionally, a Scientific Program Officer in the Extramural Research Program Office, NCHHSTP/OADS/OD will be responsible for the normal scientific and programmatic stewardship of the award as described below.

- Named in the NOA as the Program Official to provide overall scientific and programmatic stewardship of the award;
- Serves 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;
- Makes recommendations on requests for changes in scope, objectives, and/or budgets that deviate from the approved peer-reviewed application;
- Carries out continuous review of all activities to ensure objectives are being met;
- Attends committee meetings and participates in conference calls for the purposes of assessing overall

progress, and for program evaluation purposes; and
- Monitors 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: https://era.nih.gov/registration_accounts.cfm

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

Organizations may verify their current registration status by running the “List of Commons Registered Organizations” query found at: https://era.nih.gov/registration_accounts.cfm. Organizations not yet registered can go to https:// 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)
Telephone 770-488-2700
Email: PGOTIM@cdc.gov
Hours: Monday - Friday, 7am – 4:30pm U.S. Eastern Time

Program Official/ Scientific Research Contact

Amy Yang, PhD
Extramural Research Program Office
Office of the Associate Director for Science
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services
1600 Clifton Road, MS E-60
Atlanta, GA 30333
Telephone: 404-718-8836
Fax: 404-718-8822
Email: VDZ9@CDC.GOV

Peer Review Contact

Gregory Anderson, MPH, MS
Extramural Research Program Office
Office of the Associate Director for Science
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services
1600 Clifton Road, MS E-60
Atlanta, GA 30333
Telephone: 404-718-8833
Fax: 404-718-8822
Email: GAnderson@cdc.gov

Financial/Grants Management Contact

Anella Higgins
Office of Financial Resources
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services
2920 Brandy Wine Road, MS E15
Atlanta, GA 30341
Telephone: 770-488-2710
Fax: (770) 488-8350

AOH2@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.

Sections 317, 317(k)(2) of the Public Health Service Act (42 U.S.C. Sections 247b, 247b(k)(2) and 247c), as amended.

Summary of the Conference Call held on Thursday, December 3, 2015 with Potential Applicants for Funding Opportunity Announcement (FOA): IP16-002 "Annual Estimates of Influenza Vaccine Effectiveness for Preventing Medically Attended Laboratory-Confirmed Influenza in the United States."

Introductory Comments
Any scientific or technical questions should be addressed to the Scientific Program Officer, Dr. Amy Yang (AYang@cdc.gov). Any questions on financial, grants management, or eligibility aspects should be addressed to the Grants Management Officer, Ms. Anella Higgins (AOH2@cdc.gov). Questions regarding the Peer Review process should be addressed to the Scientific Review Officer, Mr. Gregory Anderson (GAnderson@cdc.gov). Contact information can be found in the FOA in Part 2, Section VII. "Agency Contacts". Information for application submission is listed in Section IV. "Application and Submission Information".

Eligibility Information
Please see Part 2, Section III. for eligibility requirements. Please also see the "Special Eligibility Requirements" for this FOA. Applications submitted under this funding opportunity announcement must not include activities that overlap with simultaneously-funded research under other awards. If a current awardee of CDC FOA IP11-003 applies to this FOA, and the application ranks sufficiently high to be awarded, funding restrictions will apply to ensure no overlap of the budget or project periods between IP11-003 and IP16-002.

Responsiveness
Please see Part 2, Section III.5. "Responsiveness" in this FOA. If the investigators plan to use their State Health Department laboratory or contract laboratory services for RT-PCR and viral cultures, then documents supporting this partnership must be submitted as part of the application.

Required Registrations
Please see Part 2, Section III.6. "Required Registrations" for information on required registrations. Please complete all registrations early. Late applications will not be accepted because of submission issues resulting from improper registrations.

Letter of Intent
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 CDC staff to estimate the potential review workload and plan the review. Letters of intent are therefore strongly encouraged. Please see Part 2, Section IV.3. "Letter of Intent" for instructions on submitting a letter of intent. Please clearly state which, if any, of the optional

components will be included in your application. Letters of intent may be sent via email to Mr. Gregory Anderson at GAnderson@cdc.gov no later than December 14th, 2015.

Application Deadline
Applications are due no later than 5:00 pm Eastern Time on January 11th, 2016. Please submit your application at least five days before the deadline to allow for error correction. No extensions will be granted for applications that are rejected because of submission errors.

Review Criteria
Applicants should pay close attention to Part 2, Section V.1. "Criteria" for information on application review criteria. The review criteria must be addressed – these are the criteria that will be used by reviewers to score the application. Failure to provide required information could result in an unfavorable score.

Application Format and Page Limitation
Please also pay close attention to Part 2, Section I.2. "Approach". Each application must address the mandatory Core Component and the two mandatory Additional Components. In addition, applications may address up to two Optional Components, but no more than one will be awarded to the same applicant. Please remember that the Research Strategy section of the Research Plan (Significance, Innovation and Approach) is limited to 25 pages for the mandatory Core plus two Additional Components, and limited to 12 pages for each of the Optional Components. Applicants should submit a budget and budget justification for each year, with the Core Component, Additional Components and Optional Component budgets and budget justifications clearly separated and identified in the application.

Number of Awards and Award Amounts
It is anticipated that there will be up to 5 awards for Mandatory Components (Core and Additional Components). It is anticipated that there will be 1 Optional Component A and up to 3 Optional Component B awards.

The estimated total funding (direct and indirect) available for Year 1 is $5,400,000 [5 sites x $800,000 (Core and Additional Components) + 1 x $500,000 Optional Component A + 3 x $300,000 Optional Component B awards]. The estimated total funding (direct and indirect) for the entire project period is $30,000,000.

Application Scoring
For this FOA, the Mandatory Components (Core and Additional Components) will be scored together as a single application and rank ordered to determine awarding of funds. Selection of applications deemed to have the highest scientific and technical merit will be based on the Overall Impact Score for the Mandatory Components.

Optional Components A and B will be scored separately from the Mandatory Components and from each other and rank ordered. Funding for the Optional Components will be limited to those applications recommended for funding of the Mandatory Components.

Questions and Answers

1. Question: Are we allowed 10 appendices for the Mandatory/Additional Components AND for EACH Optional Component?

Answer: Appendices for the Mandatory (Core and Additional) Components plus the Optional Components are limited to 10 pdfs with a total of 50 pages for all components together. Optional Components may use the "Other Attachments" section (item 12. in the "RESEARCH & RELATED Other Project Information" section of the application package) for entering the Optional Component Research Plan (Specific Aims, Research Plan, etc.).

2. Question: Given that the Optional Components are scored separately, do we upload them as separate applications?

Answer: No, you would include the Optional Component Research Plan in the "Other Attachments" section of the application (see answers to question #1 above and question #13 below).

3. Question: Should we submit a new set of biosketches, CVs, etc. for the Optional Components?

Answer: Yes - however, if there is redundancy between components, you can refer back to what you included for the Mandatory Components when describing the Optional Component section of the application.

4. Question: For Optional Component B, are you asking that we enroll 150-200 for each age group, or is that the total number for both groups?

Answer: Only one age group would be recruited in a season; a total of 150-200 people in that age group. However, the applicants should discuss how they could enroll 150-200 participants from the other age group in a different year. We hope to be able to combine data from the different sites for some of the projects.

5. Question: For the Additional Component on RSV in years 3-5, it is unclear if you would like the applicant to budget for multiplex PCR to detect RSV and other respiratory viruses or for singleplex PCR for RSV only?

Answer: The focus of this Additional Component is on RSV. We will likely restrict testing to certain to age groups – most likely focusing on older ages. You should address your response to the best of your ability. Outlining what you think is possible and within the budgetary constraints of the FOA may be useful to the reviewers.

6. Question: Do you have any preference for a singleplex assay conducted on every age group vs. a multiplex assay on only some age groups?

Answer: Neither was specified as a priority in the FOA.

7. Question: In contrast to the previously published FOA, this one states that awardees will provide data to CDC and doesn't ask the applicants to describe analytic methods. To what extent do you want a description of how the models will be set up in the application?

Answer: All applicants will follow a standard protocol for enrollment of participants and all data will be shared with CDC. CDC will do many of the multi-site analyses. However, the sites will also have an opportunity to do analyses. Think about how the reviewers might review your application with or without that information and try to write the strongest application possible.

8. Question: Do the Mandatory Components regarding RSV and pandemic planning have a page limit requirement?

Answer: The Research Strategy for the Mandatory Components (Core plus Additional Components) should be included in the 25 pages allowed.

9. Question: Are statistical analyses required beyond what is stated in the FOA?

Answer: It is up to the applicant to decide if additional statistical analyses are needed for the project proposed.

10. Question: For Optional Component A, it is unclear if CDC is looking for a fixed household cohort as opposed to a cohort that is replaced each season to maintain a fixed number of households for the course of the study?

Answer: For this option, we would like to include a cohort of households and, within that cohort, a subgroup of households with infants/young children that is a longitudinal cohort that would continue through several years. We realize that there will be some drop-outs and a need for new enrollment to maintain a steady number of households.

11. Question: Does each of the co-investigators need to be a US citizen?

Answer: It is the institution that applies, not the PI. As long as the individual is legal to work for the US institution, and the institution supports the PI, it is fine. However, Section III.2 of the FOA, "Foreign Organizations" states: "For this announcement, applicants may not include collaborators or consultants from foreign institutions."

12. Question: Can we budget for a biostatistician even though CDC will be providing analytic assistance?

Answer: Yes. If there are site-specific or project-specific needs for a biostatistician, it may be included in the budget. However, CDC will provide most of the statistical support for the study projects.

13. Question: Do you have any specific instructions regarding the format in which the Optional Component budgets should be incorporated into the application template?

Answer: For the Optional Components, applicants must submit a separate PHS398 Research Plan (which includes the Research Strategy that is limited to 12 pages), Senior/Key Person Profiles and Budget pages (Sections A-K) using the SF424 (R&R) forms. Guidance for completing the SF424 (R&R) and PHS398 forms can be found at: http://grants.nih.gov/grants/funding/424/SF424_RR_Guide_General_VerC_2014.pdf . The Research Plan, Senior/Key Person Profiles and the Budget pages will need to be submitted as attachments under Item #12 [Other Attachments] using the SF424(R&R) "Other Project Information Form" within the Core Component SF424 (R&R) application. The project lead for the Optional Component should be identified as a Co-Investigator rather than as the PI unless the project lead is the PI for both the Core and Optional Components. The Optional Component must be titled to begin with the words "Optional Component" to distinguish it from the Core Component and from the Additional Components. In addition, the total direct cost for the Optional Component must be listed under the SF424 (R&R) budget as item #8 under "Other Direct Costs" in Section F of the Core Component budget for budget periods 1 through 5. A detailed budget justification for the Optional Component for budget years 1 through 5 should be included in Section K after the Core Component/Additional Component budget justifications for each respective budget period. Start a new page for the Optional Component budget narrative. Applications that do not have the Research Plan, Senior/Key Person Profiles and the Budget pages as separate attachments for the Optional Components may not be forwarded for review or funded. Sections of the application must be titled accurately for the Mandatory Core and Additional Components as well as for the Optional Components so that they may be differentiated. The Optional Component budgets must be included in the Core/Additional Component budget for each respective budget period or the Optional Components may not be forwarded for review or funded.

14. Question: If the Dual Use Research of Concern (DURC) policy is not applicable to our proposal, do we need to include anything in the application for this?

Answer: Every application needs to include a Biohazard section and this is where you can state whether or

not DURC would be applicable to your project. In any case, DURC needs to be addressed and the application needs to indicate that there is a plan for dual use research of concern should DURC develop during the term of the grant. If your project is not using one of the 15 agents/toxins listed in the policy, but is using an agent that has the potential to cause similar harm, you are technically not covered by the policy; however, it would be prudent to recognize the harmful potential of such agents in the Biohazard section of the application, and any plans to reduce the potential harm (biosafety measures to be used), to mitigate any reviewer concerns.

15. Question: For Optional Component B, two age groups are listed, <9 and >/=65. Are we to alternate by grant year between the age groups, select one for the entire 5 years, or do both for the entire 5 years?

Answer: See Question #4 above. It is advised that the applicant propose a project with one age group for Year 1 but include information stating willingness and ability to enroll from the other age group in subsequent years.

16. Question: In Part 2, Section I.2 (Approach), subsection A (Core Component), item #4 states: "Diagnose influenza cases by virus type and subtype or lineage using a standardized, validated real-time RT-PCR assay (with probes, primers and reagents approved by CDC)." Would you please clearly define for us the level of virus subtype or lineage that is required to meet the requirements of the FOA? Is there a list or resource(s) for approved subtyping and lineage assessment assays? Specifically, would the BioFire FilmArray Respiratory Pathogen Panel or the Cepheid Flu/RSV XC assay meet the stated requirements?

Answer: The Cepheid Xpert Flu/RSV provides type information (A/B) but not subtype. It would not be adequate. The film array does provide type and subtype information. However, it does not determine B lineage. CDC will provide primers and probes and some reagents to study sites/laboratories using the CDC real-time RT-PCR.

17. Question: Will grantees need to grow influenza viruses to high titer and are those titers needed for antigenic identification?

Answer: The sites will not be asked to grow viruses to high titers. They will be asked to submit a sample of specimens into national virologic surveillance.