# Department of Health and Human Services

## Part 1. Overview Information

**Participating Organization(s)**

National Institutes of Health (NIH (http://www.nih.gov))

**Components of Participating Organizations**

National Institute of Allergy and Infectious Diseases (NIAID (https://www.niaid.nih.gov/))

**Funding Opportunity Title**

### Cohort Studies To Improve Our Understanding of Influenza Immunity, Vaccine Response and Effectiveness in Older Adults (65 years and older) (U01 Clinical Trial Not Allowed)

**Activity Code**

U01 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=u01&Search.x=0&Search.y=0&Search_Type=Activity) Research Project – Cooperative Agreements

**Announcement Type**

New

**Related Notices**

None

**Funding Opportunity Announcement (FOA) Number**

RFA-AI-20-060

**Companion Funding Opportunity**

None

**Number of Applications**

See Section III. 3. Additional Information on Eligibility.

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

93.855

**Funding Opportunity Purpose**

This initiative will support the use of longitudinal cohorts to develop greater understanding of important elements of influenza immunity that impact vaccine response and vaccine effectiveness in older adults (those 65 and older). In addition, this work will increase our understanding of how these elements relate to severe outcomes from influenza virus infection in older adults (i.e., hospitalization and death).

## Key Dates

**Posted Date**

September 30, 2020

**Open Date (Earliest Submission Date)**

January 04, 2021

**Letter of Intent Due Date(s)**

January 4, 2021

**Application Due Date(s)**

February 4, 2021
All applications are due by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on the listed date(s).
Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

**AIDS Application Due Date(s)**

Not Applicable

**Scientific Merit Review**

July 2021

**Advisory Council Review**

October 2021

**Earliest Start Date**

December 2021

**Expiration Date**

February 05, 2021

**Due Dates for E.O. 12372**

Not Applicable

## Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000),except where instructed to do otherwise (in this FOA or in a Notice from NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/)).

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.

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

# Table of Contents

# Part 2. Full Text of Announcement

## Section I. Funding Opportunity Description

### Purpose

The purpose of this Funding Opportunity Announcement (FOA) is to support research to determine how changes in immune function in individuals 65 years of age and older, including the role of pre-existing immunity to influenza generated by a history of natural infections and/or vaccinations, impact protective immunity, through characterization of existing or new longitudinal cohorts. This work will increase understanding of correlates of protection in older individuals; the impact of influenza exposure and vaccination history on protective immune responses; and immunological mechanisms associated with vaccine failure, including potential intra-seasonal waning of protection. In addition, this research may lead to the identification of risk factors for severe outcomes associated with influenza infection. Ultimately, this work will inform efforts to develop durable, broadly protective influenza vaccines across the adult age spectrum.

### Background

Influenza affects millions of people in the United States each year. Some groups are at higher risk of developing influenza-related complications requiring hospitalization that may lead to death. These high-risk individuals in these groups include pregnant women, infants and young children, older adults (≥65 years of age), residents of long-term care facilities, and those with certain chronic medical conditions (e.g., asthma, diabetes, heart disease). Older adults are particularly at risk for infection, hospitalization, and death due to influenza-related complications, such as pneumonia, and 90% of influenza-related deaths occur in older adults despite widespread vaccination programs and vaccine formulations developed specifically for older adults. The overall estimated effectiveness of seasonal influenza vaccine for preventing medically attended, laboratory-confirmed influenza infection in the U.S. was 47% for the 2018-2019 influenza season, but only 12-13% for older adults (CDC). The number of adults ages 65 and older is projected to nearly double from 52 million in 2018 to approximately 95 million in 2060 (U.S. Census Bureau). There is increasing evidence that acute influenza infection can have lasting health implications, particularly for older adults who are frail, in whom hospital admission is a known independent risk factor for decline in mobility and function. If influenza infection leaves older adults with lasting increases in frailty, the true burden of influenza may go far beyond the period of acute illness and have long-term consequences and associated healthcare requirements.

Immunosenescence (i.e., the general decline in immune function), suboptimal vaccine effectiveness, and chronic inflammation, can leave older adults more vulnerable to infection. Decline in the generation, differentiation, activation, proliferation, and cytokine profiles of T cells diminishes their ability to provide help to B cells resulting in weakened antibody titers in response to vaccination and/or infection. Reduced proportions of naïve T cells in the elderly could restrain their ability to mount *de novo* responses to antigenically drifted influenza viruses in seasonal vaccines, resulting in a greater tendency to target more conserved viral antigens and impeding immune capability. Changes are observed in aged hematopoietic stem cells (HSC), and include reduced repopulation capability, homing, and self-renewal, and a skewed differentiation toward the myeloid lineage. Age-associated dysfunction of lung-resident cells that include B cells, T cells, dendritic cells, and airway epithelial cells contribute to curtailed or suboptimal immune responses against respiratory infections. A better understanding of the mechanisms regulating aging immune responses and chronic inflammatory conditions associated with aging may provide insight into the host response to influenza infection and/or vaccination. Harnessing protective immune responses and understanding key determinants that position such responses at the site of infection would be beneficial. Thus, the development of an influenza vaccine that protects against most or all influenza viruses and provides sufficient durable protection might decrease the need for repeated seasonal immunization.

Strategies currently exist to increase vaccine effectiveness in older adults, which include higher antigen dose or inclusion of an adjuvant to better stimulate the immune system. Approaches to optimize vaccine immunogenicity for eliciting influenza-specific B and T cells and innate immune responses include modifying vaccine schedules or routes of delivery (e.g. intranasal or intradermal inoculation); adjusting vaccine dosage and composition; and adding adjuvants to increase effectiveness of vaccines in the elderly. Additionally, mechanisms to harness leukocytes recognizing conserved antigens may be used to reduce viral load and limit disease severity. Advanced technologies that provide comprehensive analyses of immune function can be used to define immune mechanisms involved in protective influenza vaccine responsiveness and efficacy in older adults. The successful immunization of older adults with the Shingrix herpes zoster vaccine points to the importance of an effective adjuvant in eliciting protective immunity in aged populations. The ability to effectively trigger

innate immune responses in older adults with effective adjuvants may provide a key insight into causes of vaccine failures and avenues toward vaccine improvement. Cohort studies enable the examination of vaccination history, intraseasonal waning, including other variables related to immune mechanism changes with aging, and their potential interactions as possible contributors towards lower vaccine effectiveness in this population.

## Research Objectives and Scope

The biological process of aging impacts multiple immune components, resulting in delayed and reduced responsiveness to vaccines and infectious agents, including influenza. Additionally, known deficiencies in vaccine-induced immune responses underscore the critical need to understand mechanisms governing innate and adaptive immune changes as they relate to influenza-specific immune outcomes. This initiative responds to this need by creating the opportunity to define immune mechanisms that contribute to: increased risk for severe outcomes for this population; suboptimal vaccine responsiveness; and durable, protective immunity that will help advance the design of an effective universal influenza vaccine in longitudinal cohorts of individuals 65 years and older.

Because many of the changes evident in the elderly may begin at younger ages (40-60 years or younger), comparisons between younger and older individuals may be included. This initiative will support an inter-disciplinary effort to generate, analyze, and integrate data from clinical research to address critical questions in influenza immunity. This program encourages the use of innovative approaches to define pathways and mechanisms that contribute to the immune status and response of older individuals who are infected with influenza and/or vaccinated with one of the licensed influenza vaccines.

This FOA requires applicants to establish new or leverage existing cohort(s) of older adults who will be followed prospectively according to any of the scenarios outlined below:

1) Older adults who have a documented clinical diagnosis of influenza infection after receiving an influenza vaccine

2) Older adults who have a documented clinical diagnosis of influenza infection but have not received an influenza vaccine

3) Older adults who have been vaccinated with an influenza vaccine and not been clinically diagnosed with influenza infection

Cohorts may include individuals from one of more of the listed scenarios, taking into consideration their vaccination and infection status during data analysis. These newly established or existing cohorts are expected to be followed for at least three (3) influenza seasons, to understand the impact of advanced age on the breadth and quality of influenza-specific innate, humoral, and T cell-mediated immune responses induced by influenza infections and/or vaccinations. Inclusion of domestic or international prospective cohorts is encouraged.

The approach taken to establish and/or expand, and characterize the cohort, including determination of the type of data and biological samples to collect, should provide the greatest degree of innovation possible to advance our understanding of rational universal influenza vaccine design.Study samples also may be included from independently-funded clinical trials or those obtained from repositories, such as the Baltimore Longitudinal Study on Aging (BLSA (https://www.blsa.nih.gov/)). Interested applicants are expected to establish collaborations with investigators responsible for these repositories prior to submitting an application to this FOA.

**Research areas of interest include but are not limited to:**

Determining the effect of an aging immune system on responses to influenza infection and/or vaccination in longitudinal cohort(s) of adults 65 years or older, including:

- Defining mechanisms of dysfunction in the aged innate immune system
- Characterizing the function and tissue-specific responses of the mucosal immune system
- Identifying age-related epigenetic or metabolic changes in aged immune cells or cells that impact influenza immunity
- Evaluating antibody titers, specificity, and function, to include changes in post-translational modifications; B cell subset generation and maintenance
- Assessing the differentiation, specificity, function/exhaustion, and maintenance of T helper, regulatory T cells, CD4 and CD8 effector and memory T cell populations
- Elucidating the impact of vaccination/influenza infection history and baseline immune status on immune response and vaccine effectiveness and immunological mechanisms associated with vaccine failure, including potential intra-seasonal waning of protection
- Identifying mechanisms by which changes in gut homeostasis and microbiome influence mucosal and systemic immune responses and inflammatory processes
- Characterizing molecular mechanisms underlying changes in immune-related autophagy with age

Evaluating differences and similarities of immune mechanisms/components elicited by influenza vaccination versus natural infection, including:

- Understanding the interactions and regulation between components of innate and adaptive immunity elicited by influenza vaccination versus natural infection that impacts acquired influenza immunity;
- Comparison of B cell and T cell receptor repertoires and responses elicited by influenza vaccination versus natural infection; and
- Comparison of the quality and functionality of antibodies induced by natural infections or vaccination.

**Applications proposing any of the following topic areas will be considered nonresponsive and will not be reviewed:**

- Those not focused on understanding the impact of aging on natural influenza infections and/or influenza vaccinations in older adults
- Any Phase clinical trials
- HIV, SIV or AIDS studies
- Animal studies
- Genome-wide association studies (GWAS)
- Behavioral research

Given the importance of the longitudinal cohort, all data generated by the funded program are expected to be deposited in the ImmPort (http://www.immport.org/immport-open/public/home/home) database (www.ImmPort.org) or other appropriate portal(s) approved by NIAID, to be made available to the scientific community. Influenza sequence data are expected to be deposited in the NIAID-supported Influenza Research Database (https://www.fludb.org/brc/home.spg?decorator=influenza).

**Steering Committee**

A Steering Committee will be established in collaboration with NIAID Program Officers to serve as the governing board of this research program.

**External Scientific Committee (ESC)**

An External Scientific (ESC) will be established by NIAID to review progress and to provide recommendations to investigators at the annual programmatic meeting. The ESC will also make recommendations regarding the continuation or re-direction of the overall research program on an ongoing basis in consultation with NIAID staff. The ESC will be established after award. Note that applicants should not contact or nominate individuals for potential ESC membership in their application.

**Annual Programmatic Meetings**

A kick-off meeting and annual program meetings will be held to establish the major roles and functions of the program and to facilitate collaborations. Additionally, annual meetings will report progress, seek new research directions and ideas, and update NIAID on issues of need. These meetings will be attended by the PD(s)/PI(s), Key personnel, NIAID staff, and the ESC membership.
See Section VIII. Other Information for award authorities and regulations.

# Section II. Award Information

**Funding Instrument**

Cooperative Agreement: A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this FOA.

**Application Types Allowed**

New
The OER Glossary (//grants.nih.gov/grants/guide/url_redirect.htm?id=11116) and the SF424 (R&R) Application Guide provide details on these application types. Only those application types listed here are allowed for this FOA.

**Clinical Trial?**

Not Allowed: Only accepting applications that do not propose clinical trials
Need help determining whether you are doing a clinical trial? (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

**Funds Available and Anticipated Number of Awards**

NIAID intends to commit $4M in FY 2022 to fund 2-4 awards.

**Award Budget**

Application budgets are not limited but need to reflect the actual needs of the proposed project.

**Award Project Period**

The maximum project period is 5 years

NIH grants policies as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this FOA.

# Section III. Eligibility Information

## 1. Eligible Applicants

### Eligible Organizations

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

The following types of Higher Education Institutions are always encouraged to apply for NIH 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
- Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Local Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)

Federal Governments

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

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Institutions)

### Foreign Institutions

Non-domestic (non-U.S.) Entities (Foreign Institutions) **are** eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

Foreign components, as defined in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are** allowed.

### Required Registrations

**Applicant organizations**

Applicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications (//grants.nih.gov/grants/guide/notice-files/NOT-OD-15-039.html) states that failure to complete registrations in advance of a due date is not a valid reason for a late submission.

- Dun and Bradstreet Universal Numbering System (DUNS) (http://fedgov.dnb.com/webform) - All registrations require that applicants be issued a DUNS number. After obtaining a DUNS number, applicants can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- System for Award Management (SAM) (https://www.sam.gov/portal/public/SAM/) – Applicants must complete and maintain an active registration, which requires renewal at least annually. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
    - NATO Commercial and Government Entity (NCAGE) Code (//grants.nih.gov/grants/guide/url_redirect.htm?id=11176) – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in order to register in SAM.
- eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Applicants must have an active DUNS number to register in eRA Commons. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration, but all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- Grants.gov – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

**Program Directors/Principal Investigators (PD(s)/PI(s))**

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

### Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) 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 NIH support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF424 (R&R) Application Guide.

### 2. Cost Sharing

This FOA does not require cost sharing as defined in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11126)

### 3. Additional Information on Eligibility

### Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see NOT-OD-11-101 (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-101.html))

## Section IV. Application and Submission Information

### 1. Requesting an Application Package

The application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional system-to-system solution. Links to apply using ASSIST or Grants.gov Workspace are available in Part 1 of this FOA. See

your administrative office for instructions if you plan to use an institutional system-to-system solution.

## 2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000) except where instructed in this funding opportunity announcement to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

### 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 IC 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:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

The letter of intent should be sent to:

Louis Rosenthal, PhD
Telephone: 240-669-5070
Email: louis.rosenthal@nih.gov (mailto:louis.rosenthal@nih.gov)

### Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits (//grants.nih.gov/grants/guide/url_redirect.htm?id=11133) must be followed.

with the following exceptions or additional requirements: For this specific FOA, the Research Strategy section is limited to 30 pages.

### Instructions for Application Submission

The following section supplements the instructions found in the SF424 (R&R) Application Guide and should be used for preparing an application to this FOA.

### SF424(R&R) Cover

All instructions in the SF424 (R&R) Application Guide must be followed.

### SF424(R&R) Project/Performance Site Locations

All instructions in the SF424 (R&R) Application Guide must be followed.

### SF424(R&R) Other Project Information

All instructions in the SF424 (R&R) Application Guide must be followed.

### SF424(R&R) Senior/Key Person Profile

All instructions in the SF424 (R&R) Application Guide must be followed.

### R&R or Modular Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

With the following additional instructions:

Funds may be requested in the budget for the PD(s)/PI(s), or other key personnel to travel and attend the kickoff and annual one-day programmatic meetings to be held in the Rockville, MD area.

Funds may be requested to support central data storage and data management for all researchers within the applicant group; and to support the timely submission of data and data analyses to the ImmPort database or other portals(s) approved by NIAID.

If needed, funds may be requested to support sample collections from clinical studies/trials that are independently funded.

### R&R Subaward Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

### PHS 398 Cover Page Supplement

All instructions in the SF424 (R&R) Application Guide must be followed.

## PHS 398 Research Plan

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

**Specific Aims:** List the broad, long-range objectives and goals of the proposed research, and indicate how these goals will be accomplished based on the longitudinal cohorts and immunological studies. Concisely describe the hypothesis or hypotheses to be tested. Indicate how the work proposed dovetails to address the overall goals and objectives of the research.

**Research Strategy**

- Describe how the PD(s)/PI(s) will establish an administrative and unifying infrastructure responsible for organizing, coordinating and providing oversight for the implementation of activities that facilitate progress and completion of the research project and support all phases of the prospective cohort establishment and analyses.
- Describe how the Principal investigator and collaborators will provide relevant input and support for cohort establishment for addressing the research hypotheses. Describe the overall management plan, including how resources will be managed, organized and prioritized, and how subcontracts and consultants, if applicable, will be selected/funded and monitored. Describe how communications will be planned, implemented and provided to collaborators. Without repeating information from individual biosketches, describe the team's experience with designing and implementing cohorts of older adults, and past accomplishments, specifically related to cohorts. In addition, describe plans to ensure efficient cooperation, communication and coordination across multiple sites, if applicable
- Describe how the selected immunologic analyses of longitudinal cohorts of older adults (age 65 or older) will determine the impact of aging on immune responses to natural influenza infections and/or influenza vaccinations.
- Describe the immunologic analyses that will be conducted to quantitate and characterize immune responses generated by influenza vaccinations or natural influenza infections.
- Describe the rationale for control groups to be included in the study.
- Describe strategies for oversight and implementation of approaches in the identification and clinical characterization of human subjects, including the clinical meta-data that will be captured, and the quality standards for data and sample collection.
- In a separate section labeled, "Data Management Plan," describe internal and external data acquisition strategies to achieve harmonization of systems and procedures for data management, data quality, data analyses, and dissemination for all of the data and data-related materials generated by the research study. Describe how uniformity of procedures and high-quality content from all study sites and the research study, in terms of the data collection, management and storage functions will be achieved. Within the plan, indicate the extent to which dedicated systems or procedures will be utilized to harmonize the acquisition, curation, management, inventory and storage of data and samples. Describe how training for the data and sample collection, in terms of the use of electronic data capture systems, will be provided to all staff including those at enrollment sites. Describe how these data taken together will address the overall goals and objectives of the research study.
- In a separate section labeled, "Statistical Analysis Plan," describe the overall plan for biostatistical support systems and personnel to perform the following functions in support of the research project, for example: 1) preliminary data analyses, 2) estimates of power and sample size, 3) research study design and development of procedures. Describe how unique and innovative approaches to statistical analysis of prospective observational cohort data will achieve the aims of the research study. Describe the plan to support the data analytics and design features unique to the research study.
- In a labeled section called, "Project Milestones", describe specific quantifiable milestones by annum, and include annual projections for the overall research study and for tracking progress from individual sites (if applicable) and collaborators. Milestones must specify the outcome(s) for each activity. Milestones should be quantifiable and scientifically justified, and include the completion of major research study activities, including, for example, protocol development, case report forms, scheduled clinical visits, obtaining clearances study completion, and analysis of final data. Milestone criteria should not simply be a restatement of the specific aims. Using a Gantt chart or equivalent tool, describe the associated timelines and identified outcomes for the research study. Within this section, consider the use of existing resources that would facilitate the progress of the project in terms of enrollment or data collection, for example, practice-based research networks, electronic medical records, administrative database, or patient registries.

**Resource Sharing Plan**: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide.

The following modifications also apply:

- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan. To promote public access to the data generated through the program, all investigators funded under this FOA will be expected to share their data through ImmPort (http://www.immport.org/immport-open/public/home/home)or other portal(s) approved by NIAID, as well as any collected biological samples. Influenza sequence data are expected to be deposited in the NIAID-supported Influenza Research Database (https://www.fludb.org/brc/home.spg?decorator=influenza). Therefore, the Resource Sharing plan should include a summary of how the applicant will manage data submission and interactions with the chosen portal(s).

- In their Data Sharing Plan, applicants are also expected to provide a timeline for the planned acceptance, quality check, transfer and upload of data of all types.

**Letters of Support:** Provide all appropriate letters of support, including any letters necessary to demonstrate the support of consortium/site participants. Include letter(s) of collaboration from investigators who have agreed to share existing cohorts and samples for this study.

## Appendix:

Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide

## PHS Human Subjects and Clinical Trials Information

When involving human subjects research, clinical research, and/or NIH-defined clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

**Study Record: PHS Human Subjects and Clinical Trials Information**

All instructions in the SF424 (R&R) Application Guide must be followed.

Section 2 - Study Population Characteristics

2.2 Eligibility Criteria

Additional Instructions

Describe in detail the inclusion and exclusion criteria for all cohorts, (elderly and control cohorts) realizing that individuals might have been previously infected with influenza or vaccinated with one or more influenza vaccines during their lifetime.

Investigators may select a younger cohort (below 65 years) as a comparison for the elderly cohort (65 years and older) and provide a rationale for the younger age range chosen.

Outline the ages for eligibility of older individuals to meet the requirements of the research objectives and for any control cohort(s), and to meet the requirement for following all enrolled cohorts for at least three (3) influenza season cycles.

2.5 Recruitment and Retention Plan

Additional Instructions

Describe how subjects for enrollment will be identified to enable implementation of the inclusion and exclusion criteria, and detail the verification process (e.g., medical record, clinical diagnostic tests) for conditions requiring verification (i.e., vaccination, influenza assay) through at least three influenza season cycles.

2.7 Study Timeline

Additional Instructions

If applicable, address the timeline for the planned enrollment process with respect to the required conditions of the subject pool.

Section 3 - Protection and Monitoring Plans

3.5 Overall Structure of the Study Team

Additional Instructions

Describe the plan to include functional working Teams with expertise in areas specific to meet the goals and objectives of the study.

**Delayed Onset Study**

Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the SF424 (R&R) Application Guide must be followed.

## PHS Assignment Request Form

All instructions in the SF424 (R&R) Application Guide must be followed.

## Foreign Institutions

Foreign (non-U.S.) institutions must follow policies described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11137), and procedures for foreign institutions described throughout the SF424 (R&R) Application Guide.

### 3. Unique Entity Identifier and System for Award Management (SAM)

See Part 1. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov

### 4. Submission Dates and Times

Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or Federal holiday (https://grants.nih.gov/grants/guide/url_redirect.html?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to Grants.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the NIH Policy on Late Application Submission.

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

Information on the submission process and a definition of on-time submission are provided in the SF424 (R&R) Application Guide.

### 5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11142)

### 6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11143).

### 7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the SF424 (R&R) Application Guide. Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit How to Apply – Application Guide (https://grants.nih.gov/grants/how-to-apply-application-guide.html). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Dealing with System Issues (https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm) guidance. For assistance with application submission, contact the Application Submission Contacts in Section VII.

**Important reminders:**

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF424(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 NIH. See Section III of this FOA for information on registration requirements.

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. Additional information may be found in the SF424 (R&R) Application Guide.

See more tips (//grants.nih.gov/grants/guide/url_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review and responsiveness by components of participating organizations, NIH. Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed.

### Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in the policy (//grants.nih.gov/grants/guide/url_redirect.htm?id=82299). Any instructions provided here are in addition to the instructions in the policy.

# Section V. Application Review Information

## 1. Criteria

Only the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the NIH mission (//grants.nih.gov/grants/guide/url_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

### Overall Impact

Reviewers will provide an overall impact 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? Is the prior research that serves as the key support for the proposed project rigorous? 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?

*Specific to this FOA:* Will the proposed research help to define mechanism(s) or increase understanding of the impact of aging on human immune responses to influenza infections and/or influenza vaccinations in older adults? Will these studies provide novel information that can be used by others to facilitate design of durable, broadly protective influenza vaccines?

#### Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, 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?

*Specific to this FOA:* How well will the PD/PI and collaborators contribute to the success of the overall cohort establishment and research study outcome? Is an appropriate coordination and unifying infrastructure in place to support all phases of the prospective cohort establishment and analyses?

#### 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?

*Specific to this FOA:* Are appropriate innovative approaches to statistical analyses of prospective observational cohort data proposed?

#### Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? 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? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as

the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?
*Specific for this FOA:*

- Are plans for the immunologic analyses appropriate and sound to facilitate attainment of the objective(s) of the proposed study?
- Does the applicant provide an adequate plan for clinical visit data, biological specimen and associated data collection procedures from the cohort, including specimen labeling, coding, tracking, storing, and inventory?
- Are the milestones for the research study feasible based on the proposed time frames? Do they provide quantifiable measures for the achievement of intended outcomes for the program as a whole in a timely manner? Does the study timeline account for engagement of multiple enrollment sites, the accurate identification and subsequent enrollment of participants, and all planned assessments and measurements on subjects (including collection of biological samples)?
- Are the research procedures adequately described, and do the consent forms provide sufficient detail to clarify the process of subject participation?
- Are the strategies for oversight and implementation of approaches in the recruitment and clinical characterization of human subjects adequate to ensure a robust clinical population sample?
- Do the data analyses plans adequately describe the study design features, and estimate power and sample size to achieve the goals of the program?
- Are the plans for data management appropriate to achieve the goals of the program?
- Is adequate justification provided for the inclusion of a younger cohort as a comparison for cohorts who are 65 years and older?

### 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?

*Specific for this FOA:* Are the IT resources and environment as described adequate to support the activities of the research study? Are the site-specific facilities purposed for biological sample storage adequate to meet the needs of the research study?

## 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 score, but will not give separate scores for these items.

### Protections for Human Subjects

For research that involves human subjects but does not involve one of the 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 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 Guidelines for the Review of Human Subjects (//grants.nih.gov/grants/guide/url_redirect.htm?id=11175).

### Inclusion of Women, Minorities, and Individuals Across the Lifespan

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research (//grants.nih.gov/grants/guide/url_redirect.htm?id=11174).

### Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. Reviewers will assess the use of chimpanzees as they would any other application proposing the use of vertebrate animals. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (//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.

### Resubmissions

Not Applicable

### Renewals

Not Applicable

### Revisions

Not Applicable

## 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 score.

### Applications from Foreign Organizations

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

### Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

### Resource Sharing Plans

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: (1) Data Sharing Plan (//grants.nih.gov/grants/guide/url_redirect.htm?id=11151); (2) Sharing Model Organisms (//grants.nih.gov/grants/guide/url_redirect.htm?id=11152); and (3) Genomic Data Sharing Plan (GDS) (//grants.nih.gov/grants/guide/url_redirect.htm?id=11153).

### Authentication of Key Biological and/or Chemical Resources:

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

### 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.

## 2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by{LOCUS OF REVIEW}, in accordance with NIH peer review policy and procedures (//grants.nih.gov/grants/guide/url_redirect.htm?id=11154), using the stated review criteria (file:///C:/Users/mckenziene/AppData/Local/Microsoft/Windows/INetCache/Content.Outlook/13V4QPZR/Research%20Draft.doc#_1._Criteria). Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications will receive a written critique.

Applications may 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 score.

Appeals (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-064.html) of initial peer review will not be accepted for applications submitted in response to this FOA.

Applications will be assigned on the basis of established PHS referral guidelines to the appropriate NIH Institute or Center. 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 by the appropriate national Advisory Council or Board. 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.

### 3. 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) via the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.
Information regarding the disposition of applications is available in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11156).

## Section VI. Award Administration Information

### 1. Award Notices

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157).
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 described in Section IV.5. 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 reimbursed only to the extent considered allowable pre-award costs.

Any application awarded in response to this FOA will be subject to terms and conditions found on the Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158) website. This includes any recent legislation and policy applicable to awards that is highlighted on this website.

Institutional Review Board or Independent Ethics Committee Approval: Grantee institutions must ensure that protocols are reviewed by their IRB or IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the awardee must provide NIH copies of documents related to all major changes in the status of ongoing protocols.

### 2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) as part of the NoA. For these terms of award, see the *NIH Grants Policy Statement* Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157) and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (//grants.nih.gov/grants/guide/url_redirect.htm?id=11159). More information is provided at Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158).

Recipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age and, in some circumstances, religion, conscience, and sex. This includes ensuring programs are accessible to persons with limited English proficiency. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. Please see https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html (https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html) and http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html (http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html).

HHS recognizes that research projects are often limited in scope for many reasons that are nondiscriminatory, such as the principal investigator's scientific interest, funding limitations, recruitment requirements, and other considerations. Thus, criteria in research protocols that target or exclude certain populations are warranted where nondiscriminatory justifications establish that such criteria are appropriate with respect to the health or safety of the subjects, the scientific study design, or the purpose of the research. For additional guidance regarding how the provisions apply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. HHS provides guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html (https://www.hhs.gov/civil-rights/for-individuals/special-

topics/limited-english-proficiency/fact-sheet-guidance/index.html) and https://www.lep.gov (https://www.lep.gov). For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53 (https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53).

- Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html (http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html).
- HHS funded health and education programs must be administered in an environment free of sexual harassment. Please see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html (https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html); https://www2.ed.gov/about/offices/list/ocr/docs/shguide.html; and https://www.eeoc.gov/eeoc/publications/upload/fs-sex.pdf (https://www.eeoc.gov/eeoc/publications/upload/fs-sex.pdf). For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm (https://grants.nih.gov/grants/policy/harassment.htm).
- Recipients of FFA must also administer their programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws. Collectively, these laws prohibit exclusion, adverse treatment, coercion, or other discrimination against persons or entities on the basis of their consciences, religious beliefs, or moral convictions. Please see https://www.hhs.gov/conscience/conscience-protections/index.html (https://www.hhs.gov/conscience/conscience-protections/index.html) and https://www.hhs.gov/conscience/religious-freedom/index.html (https://www.hhs.gov/conscience/religious-freedom/index.html).

Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at https://www.hhs.gov/ocr/about-us/contact-us/index.html (https://www.hhs.gov/ocr/about-us/contact-us/index.html) or call 1-800-368-1019 or TDD 1-800-537-7697.

In accordance with the statutory provisions contained in Section 872 of the Duncan Hunter National Defense Authorization Act of Fiscal Year 2009 (Public Law 110-417), NIH awards will be subject to the Federal Awardee Performance and Integrity Information System (FAPIIS) requirements. FAPIIS requires Federal award making officials to review and consider information about an applicant in the designated integrity and performance system (currently FAPIIS) prior to making an award. An applicant, at its option, may review information in the designated integrity and performance systems accessible through FAPIIS and comment on any information about itself that a Federal agency previously entered and is currently in FAPIIS. The Federal awarding agency will consider any comments by the applicant, in addition to other information in FAPIIS, in making a judgement about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review of risk posed by applicants as described in 45 CFR Part 75.205 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

## Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Part 75, and other HHS, PHS, and NIH 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 NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is 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 the NIH as defined below.

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

- Retaining primary responsibility for the planning, directing, and executing the proposed research study through oversight, management, and coordination of the participating sites, personnel and outcomes.
- Serving as the scientific oversight for the proposed research.
- Serving as a voting member of the Steering Committee, and accepting and implementing policies and procedures developed by the Steering Committee.
- Sharing data through ImmPort (https://www.immport.org/home) or other portals designated by NIAID.
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

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

- The NIH Project Scientist will support and encourage the recipient's activities by substantial involvement as partners and facilitators in the process without assuming responsibilities that remain with the PD(s)/PI(s).
- Coordinate NIAID staff assistance, including participation in periodic on-site monitoring with respect to compliance with Federal regulations, quality control, accuracy of data recording, sample accrual, enrollment, etc.
- Facilitate collaborations with and access to other NIAID-supported research resources and services. Serve as liaison/facilitator between the awardee and with the ImmPort (http://www.immport.org/immport-open/public/home/home) database and Influenza database.
- Review and assist in developing the operating guidelines and consistent policies for dealing with situations that require coordinated action.
- Periodically review the data generated under this award.
- Review progress towards achieving the goals of the project. Determinations for future year funding will be based on satisfactory annual progress reported in the RPPR and meeting annual milestones.
- Additionally, an agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice.

**Areas of Joint Responsibility include**:

- The PD(s)/PI(s) and NIH Project Scientist will review the program milestones annually and update the milestones in consideration with recommendations from the ESC.
- The NIH Project Scientist and the PD(s)/PI(s) will coordinate the scientific objectives and progress to facilitate the achievement of program goals.

**Dispute Resolution:**

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel composed of three members will be convened. It will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure does not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.

### 3. Reporting

When multiple years are involved, awardees will be required to submit the Research Performance Progress Report (RPPR) (//grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161)
A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161).

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. All awardees of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11170) on all subawards over $25,000. See the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11171) for additional information on this reporting requirement.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value greater than $10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of information reported in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). As required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 2011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

## Section VII. Agency Contacts

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

### Application Submission Contacts

eRA Service Desk (Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten submission by the due date, and post-submission issues)

Finding Help Online: http://grants.nih.gov/support/ (//grants.nih.gov/support/) (preferred method of contact)
Telephone: 301-402-7469 or 866-504-9552 (Toll Free)

General Grants Information (Questions regarding application instructions, application processes, and NIH grant resources)
Email: GrantsInfo@nih.gov (mailto:GrantsInfo@nih.gov) (preferred method of contact)
Telephone: 301-945-7573

Grants.gov Customer Support (Questions regarding Grants.gov registration and Workspace)
Contact Center Telephone: 800-518-4726
Email: support@grants.gov (mailto:support@grants.gov)

### Scientific/Research Contact(s)

Mercy PrabhuDas, PhD, MBA
Division of Allergy, Immunology and Transplantation (DAIT)
National Institute of Allergy and Infectious Diseases (NIAID)
Telephone: 240-627-3534
Email: mprabhudas@niaid.nih.gov (mailto:mprabhudas@niaid.nih.gov)

Michael Cooper, PhD
Division of Microbiology and Infectious Diseases (DMID)
National Institute of Allergy and Infectious Diseases (NIAID)
Telephone: 240-669-2928
Email: michael.cooper3@nih.gov (mailto:michael.cooper3@nih.gov)

### Peer Review Contact(s)

Louis Rosenthal, PhD
National Institute of Allergy and Infectious Diseases (NIAID)
Telephone: 240-669-5070
Email: louis.rosenthal@nih.gov (mailto:louis.rosenthal@nih.gov)

### Financial/Grants Management Contact(s)

Yescenia Mendoza
National Institute of Allergy and Infectious Diseases (NIAID)
Telephone: 301-627-3671
Email: yescenia.mendoza@nih.gov (mailto:yescenia.mendoza@nih.gov)

## Section VIII. Other Information

Recently issued trans-NIH policy notices (//grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

### Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 45 CFR Part 75.

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Weekly TOC for this Announcement (/grants/guide/WeeklyIndex.cfm?10-02-20)
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