U.S. Department of Health and Human Services Public Health Service
Supplemental Grant Application Instructions
For All Competing Applications and Progress Reports*

* Use for due dates on or between January 25, 2016 and May 24, 2016. **For due dates on or before January 24, 2016, use the previous version, updated November 25, 2014.**

Instructions for PHS 398, SF424 (R&R), PHS 416-1, PHS 2590, RPRR, and PHS 416-9
Rev. 06/2015, Updated 11/2015

Form Approved Through 10/31/2018
OMB No. 0925-0001 and OMB No. 0925-0002

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PART II

Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan and Human Subjects Research Policy

1. Introduction

A Protection of Human Subjects section of the Research Plan is required for all applications submitted using the PHS 398 and SF424 (R&R) instructions and forms. The information provided in the section on Protection of Human Subjects should be consistent with the information provided on the face page of the application.

For all research involving human subjects, the Scientific Review Group (SRG) will assess the adequacy of protections for research participants against research risks, and the scientifically appropriate inclusion of women, minorities, and children, based on the information provided in the application.

To assist in preparing the section on Protection of Human Subjects, six possible scenarios are provided in Section 2 below. All research projects will fall into one of these six scenarios. (To help determine whether research that involves the use of human data or biological specimens is human subjects research, refer to this Web site: http://grants.nih.gov/grants/policy/hs/.) Determine which scenario the proposed research falls into, then go to the specific instructions applicable to that scenario in Section 3. Where appropriate, Section 3 provides instructions on addressing the Inclusion of Women and Minorities, the Planned Enrollment Reports(s), and the Inclusion of Children. All definitions related to human subjects research are linked to text found in Part III.3 under Human Subjects Research Definitions and Terms. Section 5 of this Part includes descriptions of and links to the HHS Human Subjects Protections regulations and NIH policies that apply to clinical research.

Do not use the human subjects section to circumvent the page limit of the Research Strategy.

While this information is written primarily for competing applications, guidance here may also be applicable to interim progress reports.

2. Scenarios

Scenario A. No Human Subjects Research

If no human subjects research is proposed in the application, you will have designated “No” in response to Human Subjects Research on the PHS 398 face page (or on the SF424 (R&R) Other Project Information Form). 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.

See the instructions for Scenario A.

Other than a justification for using human specimens or data in the proposed research as described above, no additional information is necessary if no human subjects are involved.

Scenario B. Non-Exempt Human Subjects Research

If research involving human subjects is anticipated to take place under the award, you will have designated “Yes” in response to Human Subjects Research on the PHS 398 face page (or on the SF424 (R&R) Other Project Information Form where you will have entered your assurance number). In the Protection of Human Subjects section of the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets (1) the requirements of the HHS regulations to protect human subjects from research risks (45 CFR part 46), and (2) the requirements of NIH policies on inclusion of women, minorities, and children. Research involving a clinical trial will fall under either Scenario E or F below.

See the instructions for Scenario B.

Scenario C. Exempt Human Subjects Research

If **all** of the proposed human subjects research meets the criteria for one or more of the exemptions from the requirements in the HHS regulations (46.101(b)), "yes" should be designated in response to Human Subjects Research as well as Research Exempt on the PHS 398 face page (or **Yes** should be designated in response to "Are Human Subjects Involved?" on the SF424 (R&R) Other Project Information Form, the appropriate exemption number should be checked, and "NA" should be entered for the Human Subject Assurance Number since no OHRP assurance number is required for exempt research). In the section on Protection of Human Subjects in the Research Plan (or on the PHS Fellowship Supplemental Form for Fellowship applicants), provide a justification for the exemption(s) containing sufficient information about the involvement of the human subjects to allow a determination by peer reviewers and NIH staff that claimed exemption(s) is/are appropriate.

The PHS agency will make a final determination as to whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the Research Plan. When in doubt, consult with the Office for Human Research Protections (OHRP), Department of Health and Human Services by accessing their Web site http://www.hhs.gov/ohrp/ for guidance and further information.

The exemptions appear in Part III under Human Subjects Research Definitions and Terms.

Unless the research meets the requirements for Exemption 4, the investigator(s) must address the requirements of NIH policies on the inclusion of women, minorities, and children.

Please note: if the proposed research involves only the use of human data or biological specimens, you should first determine whether the research involves human subjects. The exemptions do not apply if the research does not involve human subjects. For help determining whether research that involves the use of human data or biological specimens is human subjects research, please refer to this Web site: http://grants.nih.gov/grants/policy/hs/.

See the instructions for Scenario C.

Scenario D. Delayed-Onset Human Subjects Research

If human subjects research is anticipated within the period of the award but plans for involvement of human subjects cannot be described in the application as allowed by the HHS regulations (45 CFR part 46.118), you will have designated "Yes" to Human Subjects Research on the PHS 398 face page (or you will have designated **Yes** in response to "Are Human Subjects Involved?" on the SF424 (R&R) Other Project Information Form and entered your OHRP assurance number). In the section on Protection of Human Subjects in the Research Plan (or on the PHS Fellowship Supplemental Form for Fellowship applicants), you should either include an explanation of anticipated protections for human subjects or an explanation of why protections cannot be described.

Examples of delayed-onset of human subjects research include:

- Human subjects research is dependent upon the completion of animal or other studies; or
- Human subjects research protocols to be included will be determined at a later time after award; (often defined by a FOA).

See instructions for Scenario D.

Scenario E. Human Subjects Research Involving a Clinical Trial

If research involving human subjects is anticipated to take place under the award, and you intend to conduct a clinical trial characterized to include

a) Prospective assignment of human subjects;

b) One or more intervention, and;

c) Identification of one or more health-related biomedical or behavioral outcomes during the project period, you will have designated "Yes" in Human Subjects Research on the PHS 398 face page,

"No" in in response to Research Exempt on the PHS 398 face page, and "Yes" in response to Clinical Trial on the PHS 398 face page (or you will have designated **Yes** in response to "Are Human Subjects Involved?" on the SF424 (R&R) Other Project Information Form, entered your OHRP assurance number, and checked "Yes" to Clinical Trial on either the PHS 398 Cover Page Supplement Form or on the PHS Fellowship Supplemental Form).

In the section on Protection of Human Subjects in the Research Plan (or on the PHS Fellowship Supplemental Form for Fellowship applicants), you must provide sufficient information for reviewers to determine that the proposed research meets:

1) the requirements of the HHS regulations to protect human subjects from research risks (45 CFR part 46);
2) the NIH policy requirements for Data and Safety Monitoring for Clinical Trials;
3) the ClinicalTrials.gov requirements if applicable;
4) the requirements of NIH policies on inclusion of women, minorities, and children; and
5) the requirements of NIH policy on reporting race and ethnicity data for human subjects in NIH-defined clinical research.

See instructions for Scenario E.

Scenario F. Human Subjects Research Involving an NIH-Defined Phase III Clinical Trial

If research involving human subjects is anticipated to take place under the award, and you intend to conduct an NIH-defined Phase III clinical trial during the project period, you will have designated "Yes" in response to Human Subjects Research on the PHS 398 face page, "No" in response to Research Exempt on the PHS 398 face page, and "Yes" in response to NIH-defined Phase III Clinical Trial on the PHS 398 face page (or you will have designated **Yes** in response to "Are Human Subjects Involved?" on the SF424 (R&R) Other Project Information Form, entered your OHRP assurance number, and checked "Yes" to Agency-Defined Phase III Clinical Trial on the PHS 398 Cover Page Supplement Form on the PHS Fellowship Supplemental Form). In the section on Protection of Human Subjects in the Research Plan (on the PHS Fellowship Supplemental Form for Fellowship applicants), you must provide sufficient information for reviewers to determine that the proposed research meets:

1) the requirements of the HHS regulations to protect human subjects from research risks (45 CFR part 46);
2) the NIH policy requirements for Data and Safety Monitoring for Clinical Trials;
3) the ClinicalTrials.gov requirements if applicable;
4) the requirements of NIH policies on inclusion of women, minorities, and children;
5) the requirements of NIH policy on reporting race and ethnicity data for subjects in NIH-defined clinical research; and
6) additional requirements for NIH-defined Phase III clinical trials.

See instructions for Scenario F.

3. Instructions for Preparing the Section on Protection of Human Subjects

Scenario A. No Human Subjects Research Proposed

Criteria

Human Subjects Research	No

Exemption Claimed	No
Clinical Trial	N/A
NIH-Defined Phase III Clinical Trial	N/A

Instructions and Required Information

If proposed studies using human data or biological specimens do not involve human subjects, provide an explanation of why the proposed studies do not constitute research involving human subjects.

In the application narrative for paper PHS398 applications, create a heading labeled "Protection of Human Subjects" and include the following statement below the heading: "No Human Subjects Research is proposed in this application." For electronic SF424 (R&R) applications, save this explanation as a .pdf file entitled "Human Subjects Research.pdf" and attach at the "Protection of Human Subjects" item of the PHS 398 Research Plan (for K applicants, this is located on the PHS 398 Career Development Award Supplemental Form; for F applicants, on the PHS Fellowship Supplemental Form – Research Training Plan).

The explanation should include: a description of the source of the data/biospecimens and whether there is any intervention or interaction with the subjects in order to obtain the specimens and data; what identifiers will be associated with the human specimens and data and who has access to subject identities; the role(s) of providers of the data/biological specimens in the proposed research; and the manner by which the privacy of research participants and confidentiality of data will be protected.

Research that does not involve intervention or interaction with living individuals, or identifiable private information, is not human subjects research (see Definitions in Part III.3). Research involving the use of coded private information or biological specimens may not constitute human subjects research if the conditions of the OHRP Guidance on Research Involving Coded Private Information or Biological Specimens have been met (http://www.hhs.gov/ohrp/policy/cdebiol.html).

Research that only proposes the use of cadaver specimens is not human subjects research because human subjects are defined as "living individuals." The use of cadaver specimens is not regulated by 45 CFR part 46, but may be governed by other Federal, State or local laws.

Scenario B. Non-Exempt Human Subjects Research

Criteria

Human Subjects Research	Yes
Exemption Claimed	No
Clinical Trial	No
NIH-Defined Phase III Clinical Trial	No

Instructions and Required Information

Although no specific page limitation applies to this section of the application, be succinct.

In the application narrative for paper PHS398 applications, create a section entitled "Protection of Human Subjects" and create a subheading for each of the following items. For electronic SF424 (R&R) applications, provide the required information as a separate file (for K applicants, the PHS 398 Career Development Award Supplemental Form; for F applicants, the PHS Fellowship Supplemental Form – Research Training Plan). For SF 424 (R&R) applications using Forms C application packages, Protection of Human Subjects, Inclusion of Women and Minorities, and Inclusion of Children remain an upload in the Research Plan Form. However, the Planned Enrollment Report is now a separate Form in the application package.

Follow the instructions that are identified for each of the following topics and provide the required information:

Protection of Human Subjects - Section 4.1 - 4.1.4

Inclusion of Women and Minorities - Section 4.2

Planned Enrollment Reports(s) - Section 4.3

Inclusion of Children - Section 4.4

If the research involves collaborating sites or subprojects, provide the information identified above for each participating site.

Scenario C: Human Subjects Research Claiming Exemption 1, 2, 3, 4, 5, or 6

Criteria

Human Subjects Research	Yes
Exemption Claimed	1, 2, 3, 4, 5, or 6
Clinical Trial	Yes or No
NIH-Defined Phase III Clinical Trial	No

Instructions and Required Information

Although no specific page limitation applies to this section of the application, be succinct. The exemptions appear in Part III under Human Subjects Research Definitions and Terms.

Although the research may be exempt from the HHS regulatory requirements, it is still research involving human subjects and the application must follow the instructions that are identified for each of the following topics and provide the information that is requested.

In the application narrative for paper PHS398 applications, provide the required information for each of the following topics below. For electronic SF424 (R&R) applications, provide the required information for each of the following topics below as a separate file (for K applicants, the PHS 398 Career Development Award Supplemental Form; for F applicants, the PHS Fellowship Supplemental Form - Research Training Plan). For SF 424 (R&R) applications using Forms C application packages, Protection of Human Subjects, Inclusion of Women and Minorities, and Inclusion of Children remain an upload in the Research Plan Form. However, the Planned Enrollment Report is now a separate Form in the application package.

Protection of Human Subjects - Include the following statement: "This Human Subjects Research falls under Exemption(s) …" Clearly identify which exemption(s) (1, 2, 3, 4*, 5, or 6) you are claiming and justify why the research meets the criteria for the exemption(s) that you have claimed. This justification should explain how the proposed research meets the criteria for the exemption claimed and should not merely repeat the criteria or definitions themselves.

If the research will include a clinical trial, characterized to include

a) Prospective assignment of one or more human subjects;

b) One or more intervention (which can include placebo or other control); and

c) Evaluation of the effects of the intervention on one or more health-related biomedical or behavioral outcomes even if exempt, include a Data and Safety Monitoring Plan – Section 4.1.5, and address the ClinicalTrials.gov requirements if applicable – Section 4.1.6.

Inclusion of Women and Minorities - Section 4.2

Planned Enrollment Report(s) - Section 4.3

Inclusion of Children - Section 4.4

*NOTE: If all of the proposed research meets the criteria for Exemption 4, then the requirements for inclusion of women and minorities, planned enrollment report(s), and inclusion of children, do not need to be addressed.

Scenario D: Delayed-Onset Human Subjects Research

Criteria

Human Subjects Research	Yes
Exemption	Yes or No
Clinical Trial	Yes or No
NIH-Defined Phase III Clinical Trial	Yes or No

Instructions and Required Information

In rare situations, applications are submitted with the knowledge that human subjects will be involved during the period of support, but plans are so indefinite that it is not possible to describe the involvement of human subjects in the application. The kinds of activities that lack definite plans are often institutional awards where the selection of specific projects is the institution's responsibility, research training grants, and projects in which the involvement of human subjects depends upon completion of instruments, animal studies, or purification of compounds.

If the involvement of human subjects cannot be fully described, create a heading entitled “Protection of Human Subjects” and provide a detailed explanation why it is not possible to develop definite plans at this time. The explanation should be specific and directly related to the Specific Aims in the application. If the involvement of human subjects depends upon information that is not presently available (e.g., completion of instruments, animal studies, purification of compounds), be explicit about the information and the factors affecting the availability of the information. Describe the information that will be necessary in order to develop definite plans for the involvement of human subjects, why that information is not currently available, and when the information is expected to become available during the course of the project.

If an award is made, prior to the involvement of human subjects the grantee must submit to the NIH awarding office for prior approval either (1) detailed information as required in the Research Plan, Protection of Human Subjects (addressing risks to the subjects, adequacy of protection against risks, potential benefits of the proposed research, importance of the knowledge to be gained, and data and safety monitoring plan, if applicable) and certification of IRB approval, OR (2) if all of the research meets the criteria for one or more exemptions, identification of which exemption(s) is/are applicable to the research, and a justification for the exemption with sufficient information about the involvement of human subjects to allow a determination that the claimed exemption is appropriate. For NIH-defined clinical research, the request for prior approval must also address plans for the inclusion of women and minorities, the inclusion of children, and provide completed Planned Enrollment Report(s) as required in the Research Plan.

Under no circumstance may human subjects be involved in research until approval is granted by the awarding entity, and certification of IRB approval has been accepted by the agency. Inclusion plans and inclusion enrollment report(s) must also be submitted to the agency prior to starting human subjects studies.

In the application narrative for paper PHS398 applications, create a section entitled Protection of Human Subjects and a subheading for each of the following items. For electronic SF424 (R&R) applications, provide the required information for each of the following topics below as a separate file (for K applicants, the PHS 398 Career Development Award Supplemental Form; for F applicants, the PHS Fellowship Supplemental Form - Research Training Plan). For SF 424 (R&R) applications using Forms C application packages, Protection of Human Subjects, Inclusion of Women and Minorities, and Inclusion of Children remain an upload in the Research Plan Form. However, the Planned Enrollment Report is now a separate Form in the application package.

Follow the instructions that are identified for each of the following topics and EITHER provide as much of the information that is requested as possible, OR describe why it is not possible to provide the information due to delayed-onset of human subjects research:

Protection of Human Subjects - Section 4.1 - 4.1.4

If the research will include a clinical trial, characterized to include

a) Prospective assignment of one or more human subjects;

b) One or more intervention (which can include placebo or other control), and;

c) Evaluation of the effects of the intervention on one or more health-related biomedical or behavioral outcomes, include a Data and Safety Monitoring Plan - Section 4.1.5, and address the ClinicalTrials.gov requirements if applicable – Section 4.1.6.

Inclusion of Women and Minorities - Section 4.2

Planned Enrollment Report(s) - Section 4.3

Inclusion of Children - Section 4.4

Scenario E: Clinical Trial

Criteria

Human Subjects Research	Yes
Exemption	Yes or No
Clinical Trial	Yes
NIH-Defined Phase III Clinical Trial	No

Instructions and Required Information

In the application narrative for paper PHS398 applications, create a section entitled “Protection of Human Subjects” and include the following statement below the heading: “This Human Subjects Research meets the definition of a clinical trial.” (See definition of "clinical trial" under Part III.3.) Create a subheading for each of the following items below. For electronic SF424 (R&R) applications, provide the required information for each of the following topics below as a separate file (for K applicants, the PHS 398 Career Development Award Supplemental Form; for F applicants, the PHS Fellowship Supplemental Form - Research Training Plan). For SF 424 (R&R) applications using Forms C application packages, Protection of Human Subjects, Inclusion of Women and Minorities, and Inclusion of Children remain an upload in the Research Plan Form. However, the Planned Enrollment Report is now a separate Form in the application package.

Follow the instructions that are identified for each of the following topics and provide the required information:

Protection of Human Subjects - Section 4.1 - 4.1.6 (including a plan for Data and Safety Monitoring for Clinical Trials and the ClinicalTrials.gov requirements, if applicable)

Inclusion of Women and Minorities - Section 4.2

Planned Enrollment Report(s) - Section 4.3

Inclusion of Children - Section 4.4

If the research involves collaborating sites or subprojects, provide the information identified above for each participating site.

Scenario F: NIH Defined Phase III Clinical Trial

Criteria

Human Subjects Research	Yes
Exemption	No
Clinical Trial	Yes
NIH-Defined Phase III Clinical Trial	Yes

Instructions and Required Information

In the application narrative for paper PHS398 applications, create a section entitled “Protection of Human Subjects” and include the following statement below the heading: “This Human Subjects Research involves an NIH-Defined Phase III Clinical Trial.” (See definition of "NIH defined Phase III Clinical Trial" in Part III.3.). Create a subheading for each of the items below. For electronic SF424 (R&R) applications, provide the required information for each of the following topics below as a separate file (for K applicants, the PHS 398 Career Development Award Supplemental Form; for F applicants, the PHS Fellowship Supplemental Form - Research Training Plan). For SF 424 (R&R) applications using Forms C application packages, Protection of Human Subjects, Inclusion of Women and Minorities, and Inclusion of Children remain an upload in the Research Plan Form. However, the Planned Enrollment Report is now a separate Form in the application package.

Follow the instructions that are identified for each of the following topics and provide the required information:

Protection of Human Subjects - Section 4.1 - 4.1.6 (including a plan for Data and Safety Monitoring for Clinical Trials and the ClinicalTrials.gov requirements, if applicable)

Inclusion of Women and Minorities - Section 4.2

Additional Instructions and Requirements when NIH-Defined Phase III Clinical Trials are Proposed - Section 4.2.1

Planned Enrollment Report(s) - Section 4.3

Inclusion of Children - Section 4.4

If the research involves collaborating sites or subprojects, provide the information identified above for each participating site.

4. Instructions Pertaining to Non-Exempt Human Subjects Research

In your application narrative for paper PHS398 applications, create a section entitled “Protection of Human Subjects.” For applications using SF 424 (R&R) Forms C application packages, Protections of Human Subjects, Inclusion of Women and Minorities, and Inclusion of Children remain an upload in the Research Plan Form. However, the Planned Enrollment Report is now a separate Form in the application package. Although no specific page limitation applies to this section of the application, be succinct. Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the protection of human subjects. HHS regulations and policies governing human subjects research are described and referenced in Section 5 below. Use subheadings to address the issues listed under items 4.1-4.4 below. If your research includes a clinical trial, include a subheading "Data and Safety Monitoring Plan" and follow the instructions in 4.2 below. If your research includes an NIH-Defined Phase III Clinical Trial, follow the additional instructions in 4.2.1 below.

4.1 Protection of Human Subjects

4.1.1 Risks to Human Subjects

a. ***Human Subjects Involvement, Characteristics, and Design***

- Describe and justify the proposed involvement of human subjects in the work outlined in the Research Strategy section.
- Describe the characteristics of the subject population, including their anticipated number, age range, and health status, if relevant.
- Describe and justify the sampling plan, including retention strategies and the criteria for inclusion or exclusion of any subpopulation.
- Explain the rationale for the involvement of special vulnerable populations, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. Note that 'prisoners' includes all subjects involuntarily incarcerated (for example, in detention centers) as well as subjects who become incarcerated after the study begins.
- If relevant to the proposed research, describe procedures for assignment to a study group. As related to human subjects protection, describe and justify the selection of an intervention's dose, frequency and administration.
- List any collaborating sites where human subjects research will be performed, and describe the role of those sites and collaborating investigators in performing the proposed research. Explain how data from the site(s) will be obtained, managed, and protected.

b. ***Sources of Materials***

- Describe the research material obtained from living individuals in the form of specimens, records, or data.
- Describe any data that will be collected from human subjects for the project(s) described in the application.
- Indicate who will have access to individually identifiable private information about human subjects.
- Provide information about how the specimens, records, and/or data are collected, managed, and protected as well as whether material or data that include individually identifiable private information will be collected specifically for the proposed research project.

c. ***Potential Risks***

- Describe all the potential risks to subjects posed by participation in the research (physical, psychological, financial, legal, or other), and assess their likelihood and seriousness to the human subjects.
- Where appropriate, describe alternative treatments and procedures, including the risks and potential benefits of the alternative treatments and procedures, to participants in the proposed research.

4.1.2 Adequacy of Protection Against Risks

a. ***Recruitment and Informed Consent***

- Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.

- Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver. Informed consent document(s) need not be submitted to the PHS agencies unless requested.

b. ***Protections Against Risk***

- Describe planned procedures for protecting against or minimizing potential risks, including risks to privacy of individuals or confidentiality of data, and assess their likely effectiveness.
- Research involving vulnerable populations, as described in the HHS regulations, Subparts B-D must include additional protections. Refer to HHS regulations, and OHRP guidance:
    - Additional Protections for Pregnant Women, Human Fetuses and Neonates: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartb
    - Additional Protections for Prisoners: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc
    - OHRP Subpart C Guidance: http://www.hhs.gov/ohrp/policy/index.html#prisoners
    - Additional Protections for Children: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd
    - OHRP Subpart D Guidance: http://www.hhs.gov/ohrp/policy/index.html#children
- Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve clinical trials (See definition of "clinical trial" under Part III.3) must include a general description of the plan for data and safety monitoring of the clinical trials and adverse event reporting to the IRB, the DSMB (if one has been established for the trial), the NIH and others, as appropriate, to ensure the safety of subjects.

4.1.3 Potential Benefits of the Proposed Research to Human Subjects and Others

- Discuss the potential benefits of the research to research participants and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to research participants and others.
- Please note that financial compensation of subjects is not considered to be a benefit of participation in research.

4.1.4 Importance of the Knowledge to be Gained

- Discuss the importance of the knowledge to be gained as a result of the proposed research.
- Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

NOTE: Test articles (investigational new drugs, devices, or biologics) including test articles that will be used for purposes or administered by routes that have not been approved for general use by the Food and Drug Administration (FDA) must be named. State whether the 30-day interval between submission of applicant certification to the FDA and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the FDA, and/or the status of requests for an Investigational New Drug (IND) or Investigational Device Exemption (IDE) covering the proposed use of the test article in the Research Plan.

4.1.5 Data and Safety Monitoring Plan

The NIH Data and Safety Monitoring Policy is described and referenced in Section 5.3.

- If the proposed research includes a clinical trial (See definition of "clinical trial" under Part III.3), create a heading entitled "Data and Safety Monitoring Plan."
- Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring. Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the Institutional Review Board (IRB) and the funding IC, also if necessary, the DSMB (if one has been established for the trial), the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA) in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations. Be succinct. Contact the FDA (http://www.fda.gov/) and also see the following Web sites for more information related to IND and IDE requirements:
  http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr312_01.html (IND)
  http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr812_01.html (IDE)
- The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:
  - PD/PI (required)
  - Institutional Review Board (IRB) (required)
  - Independent individual/safety officer
  - Designated medical monitor
  - Internal Committee or Board with explicit guidelines
  - Data and Safety Monitoring Board (DSMB). NIH specifically requires the establishment of Data and Safety Monitoring Boards (DSMBs) for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally for Phase III clinical trials. Although Phase I and Phase II clinical trials may also need DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.
- A detailed Data and Safety Monitoring Plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects. For additional guidance on creating this Plan see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html.

4.1.6 ClinicalTrials.gov Requirements

Public Law 110-85 (also known as the FDA Amendments Act (FDAAA) of 2007) mandates registration and results reporting of "applicable clinical trials" in ClinicalTrials.gov. Under the statute these trials generally include: (1) Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation; and (2) Trials of Devices: Controlled trials with health outcomes, other than small feasibility studies, and pediatric postmarket surveillance. Review the statutory definition of applicable clinical trial to identify if registration is required to comply with the law (See PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(1)(A)).

NIH encourages registration of ALL clinical trials whether required under the law or not. On January 28, 2015, NCI published a policy requiring the reporting of final trial results in a publicly accessible manner within 12 months of the trials primary completion date. NIH is considering a policy to require all NIH supposed trials to be registered and final data reported in ClinicalTrials.gov; any final policy about this will be published in the NIH Guide for Grants and Contracts.

When registering clinical trials in the ClinicalTrials.gov Protocol Registration System, if applicable, enter the NIH Grant Number associated with the trial in the "Secondary ID" field; include activity code, institute code and 6-digit serial number (example: R01CA054321).

Registration is accomplished at the ClinicalTrials.gov Protocol Registration System Information Web site (http://prsinfo.clinicaltrials.gov/). A unique identifier called an NCT number, or ClinicalTrials.gov registry number, will be generated during the registration process.

The NIH implementation of FDAAA requires:

- the registration of applicable clinical trials in ClinicalTrials.gov no later than 21 days after the first subject is enrolled,
- the reporting of summary results information (including adverse events) no later than 1 year after the completion date for registered applicable clinical trials involving drugs that are approved under section 505 of the Food, Drug and Cosmetic Act (FDCA) or licensed under section 351 of the PHS Act, biologics, or of devices that are cleared under section 510k of FDCA, and
- if an "applicable clinical trial" is funded in whole or in part by an NIH grant or cooperative agreement, grant and progress report forms shall include a certification that the responsible party has made all required submissions to ClinicalTrials.gov.

For competing new and renewal applications that include applicable clinical trials which require registration and results reporting under FDAAA, provide the NCT number/s in the human subjects section of the Research Plan under a section heading entitled ClinicalTrials.gov.

The entity responsible for registering the trial is the "responsible party". The statute defines the responsible party as:

(1) the sponsor of the clinical trial (as defined in 21 CFR 50.3) (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=50.3), or

(2) the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee (provided that "the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements" for submitting information under the law) (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid =f:publ085.110.pdf). See PL 110-85, Section 801(a), (adding new 42 U.S.C. 282(j)(1)(A)(ix)).

For the complete statutory definitions of "responsible party" and "applicable clinical trial," refer to Elaboration of Definitions of Responsible Party and Applicable Clinical Trial.

The signature on the application of the Authorized Organization Representative assures compliance with FDAAA.

Additional information can be found on the ClinicalTrials.gov Web site (http://grants.nih.gov/ClinicalTrials_fdaaa/).

4.2 Inclusion of Women and Minorities

Create a section heading entitled "Inclusion of Women and Minorities" and place it immediately following the "Protection of Human Subjects" section. Although no specific page limits apply to this section of the application, be succinct. This section does not take the place of considering relevant biological variables (such as sex) in the research strategy. The NIH Policy on the Inclusion of Women and Minorities in Clinical Research is described and referenced in Section 5.6. Additional information and guidance can be found at: http://grants.nih.gov/grants/funding/women_min/women_min.htm.

Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the scientifically justified inclusion (or exclusion) based on sex/gender, race, and ethnicity in NIH-defined clinical

research. This section is required for all studies meeting the NIH definition for clinical research, not just clinical trials. It is important to provide a detailed plan of who will be included (and/or excluded) and how the distributions of individuals on the basis of sex/gender, race, and ethnicity are justified in the context of the scientific goals of the application. Simply stating that certain individuals will not be excluded or that individuals of either sex/gender or any race/ethnicity are eligible is not sufficient. Details about why the individuals are the appropriate individuals to accomplish the scientific goals of the study should be provided.

In this section of the Research Plan, address, at a minimum, the following four points:

1. Describe the planned distribution of subjects by sex/gender, race, and ethnicity for each proposed study and complete the format in the Planned Enrollment Report. (Instructions for completing this form are in Section 5.8 of the SF424 application package and below in Section 4.3 of these Supplemental Instructions.)
2. Describe the subject selection criteria and rationale for selection of sex/gender, racial, and ethnic group members in terms of the scientific objectives and proposed study design. The description may include, but is not limited to, information on the population characteristics of the disease or condition under study.
3. Provide a compelling rationale for proposed sample specifically addressing exclusion of any sex/gender, racial, or ethnic group that comprises the population under study.
4. Describe proposed outreach programs for recruiting sex/gender, racial, and ethnic group members as subjects. This is particularly important if difficulty recruiting certain groups is anticipated.

Additional Considerations for justifying inclusion:

There may be reasons why the proposed sample is limited by sex/gender, race, and/or ethnicity. This should be addressed as part of the four points detailed above.

- inclusion of certain individuals would be inappropriate with respect to their health;
- the research question addressed is only relevant to certain groups or there is a gap in the research area;
- evidence from prior research strongly demonstrates no difference on the basis of sex/gender, race, and/or ethnicity;
- sufficient data already exist with regard to the outcome of comparable studies in the excluded group(s) and duplication is not needed in this study;
- a certain group or groups is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects (e.g., uniquely valuable stored specimens or existing datasets are limited by sex/gender, race, and/or ethnicity; very small numbers of subjects are involved; or overriding factors dictate selection of subjects, such as matching of transplant recipients, or availability of rare surgical specimens); and/or
- representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or data-sets with incomplete sex/gender documentation are used), and this does not compromise the scientific objectives of the research.
- In general, the cost of recruiting certain groups and/or geographic location alone are not acceptable reasons for exclusion of particular groups. This should be considered when developing outreach plans. Establishing collaborations or other arrangements to recruit may be necessary.

Additional guidance for research utilizing existing datasets or resources:

- Inclusion must be addressed when conducting NIH-defined clinical research, even if the samples or data have already been collected as part of a different study. Details about the sex/gender, race, and ethnicity composition of the existing dataset/resource should be provided and justified as appropriate to the scientific goals of the proposed study.
- For the purposes of inclusion policy, an existing dataset may be constructed of different types of data including but not limited to survey data, demographic information, health information, genomic

information, etc. Also included would be data to be derived from existing samples of cells, tissues, or other types of materials that may have been previously collected for a different purpose or research question but will now be used to answer a new research question. In general, these will be studies meeting the NIH definition for clinical research with a prospective plan to analyze existing data and/or derive data from an existing resource and where no ongoing or future contact with participants is anticipated. More information about what is considered an existing dataset or resource for inclusion policy is available here.

- For an existing dataset or specimens, you may use the Cumulative Inclusion Enrollment Report rather than the Planned Enrollment Report. Additional guidance is available under Section 4.3.

4.2.1 Additional Instructions and Requirements When NIH-Defined Phase III Clinical Trials Are Proposed

If the proposed research includes an NIH-Defined Phase III Clinical Trial, the section on Inclusion of Women and Minorities also MUST address plans for how sex/gender, race, and ethnicity will be taken into consideration in the design and valid analysis of the trial. Valid analysis means an unbiased assessment which will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect.

Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the scientifically justified inclusion plans, including these additional requirements for NIH-defined Phase III clinical trials.

- Applicants should address the following issues for ensuring valid analyses:
  - inclusive eligibility criteria – in general, the cost of recruiting certain groups and/or geographic location alone are not acceptable reasons for exclusion of particular groups;
  - allocation of study participants of both sexes/genders (males and females) and from different racial and/or ethnic groups to the intervention and control groups by an unbiased process such as randomization;
  - unbiased evaluation of the outcome(s) of study participants; and
  - use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects by sex/gender, race, and/or ethnicity, particularly if prior evidence strongly suggests that differences exist.
- Applicants also should address whether they plan to test or not test for differences in effect among sex/gender, racial, and/or ethnic groups and why that is or is not appropriate. This may include supporting evidence and/or data derived from animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies as well as observational, natural history, epidemiology and/or other relevant studies. Additional factors may include planned primary and secondary outcomes and whether there are previous studies that support or negate the likelihood of differences between groups.
- The plans must include selection and discussion of one of the following analysis plans:
  - Plans to conduct analyses to detect significant differences in intervention effect among sex/gender, racial, and/or ethnic subgroups when prior studies strongly support these significant differences among one or more subgroups, or
  - Plans to include and analyze sex/gender, racial, and/or ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups. (Representation of sex/gender, racial, and ethnic groups is not required as subject selection criteria, but inclusion is encouraged.), or

- Plans to conduct valid analyses of the intervention effect in sex/gender, racial, and/or ethnic subgroups (without requiring high statistical power for each subgroup) when the prior studies neither support nor negate significant differences in intervention effect among subgroups.

4.3 Instructions for Completing the Enrollment Report(s) for Sex/Gender, Race, and Ethnicity

The NIH Policy on the Inclusion of Women and Minorities in Clinical Research is described in Part II, Section 5.6. The NIH Policy on Reporting Race and Ethnicity Data for Subjects in Clinical Research is described and referenced in Section 5.8.

Instructions for Completing Planned Enrollment Reports

(http://grants.nih.gov/grants/funding/phs398/phs398.html for paper applications SF424 (R&R) Application Guide for NIH and Other PHS Agencies, Section 5.8 for electronic applications using Forms C)

In addition to providing inclusion plans (per Section 4.2), applicants are instructed to provide the distribution of participants by sex/gender, racial, and ethnic categories using the PHS Inclusion Enrollment Report(s). See below for additional guidance on how to complete the PHS 398 Inclusion Enrollment Report form.

When completing each Planned Enrollment Report:

- Provide a unique study title that will facilitate identification of each Planned Enrollment Report.
- Select whether the study involves domestic or foreign subjects.

Provide the information as numbers of subjects, not percentages.

The Total Field on the Planned Enrollment Report (bottom right) means the number of subjects that are expected to be enrolled in the study, consistent with the definition in ClinicalTrials.gov.

Provide the numeric distribution of individuals on the basis of their sex/gender, ethnicity, and race. Note that Hispanic/Latino is an ethnic category, not a racial category, and subjects should identify both ethnicity and race. Subjects are permitted to select more than one race. If the sample is likely to include individuals who identify with more than one race, they should be accounted for in the "More than one race" category on the Planned Enrollment Report(s). If including individuals identifying as more than one race is not expected, enter zeroes in that category.

Any proposed racial or ethnic subpopulations may be listed in the comment field.

Where to Attach Planned Enrollment Report(s)

For electronic SF424 (R&R) applications using the Forms C package, if your application includes Planned Enrollment Reports, these will be entered into a structured data form(s). For paper PHS 398 applications, if your application inclusion includes Planned Enrollment Report(s), these will be inserted after the section describing plans for the inclusion of women and minorities.

If the application includes a study recruiting subjects at more than one site/location, investigators may create one Planned Enrollment Report or separate Planned Enrollment Reports (per site), depending on the scientific goals of the study and whether monitoring of inclusion enrollment would benefit from being combined or separated.

If you are preparing a multi-project application, include the Planned Enrollment Report(s) with the component that involves the study unless otherwise directed by the FOA. Should your study span more than one subproject, include the Planned Enrollment Report(s) with only one subproject and insert a comment in the comment field to indicate what other subprojects it is associated with.

For paper PHS398 applications if your application involves subprojects, attach the Planned Enrollment Reports to the relevant component immediately after the section describing the plans for the inclusion of women and minorities.

NOTE: It is important that the Planned Enrollment Report(s) for a given study only be associated with one application and provided only once in a given application. If you are submitting a single application as part of a network or set of linked applications, please provide the Planned Enrollment Report(s) with the individual site applications unless otherwise directed by the FOA.

Additional Guidance

For additional information and FAQs related to inclusion policy and inclusion enrollment forms, please see: http://grants.nih.gov/grants/funding/women_min/women_min.htm.

Renewal, Resubmission, and Revision Applications

For Renewal applications, investigators should provide information on cumulative enrollment from the previous funding period(s) as part of the progress report section of the application. The Cumulative Inclusion Enrollment Report must be used for reporting actual accrual data to the NIH. Where possible, include the Study Title that is associated with inclusion data from the previous funding period. If inclusion enrollment from the previous funding period was reported on separate cumulative inclusion enrollment reports, provide them in the same way. In addition, if a given study will continue with the same enrollment or additional enrollment, or if new studies are proposed, provide a new Planned Enrollment Report for each.

For Resubmission applications, if Enrollment Report(s) (Planned or Cumulative) were provided in the initial submission application and those studies will be part of the resubmission application, please submit again with the revision application, regardless of whether the enrollment has changed or not. Also, any new (additional) Planned Enrollment Report(s) should be provided.

For Revision applications, investigators should provide a Planned Enrollment Report(s) if new studies are planned as part of the Revision and they meet the NIH definition for clinical research.

Research Conducted with Existing Datasets

Any application (New, Renewal, Resubmission, Revision) using existing datasets or specimens that meet the NIH definition for clinical research, you may complete either the Planned Enrollment Report or the Cumulative Inclusion Enrollment Report depending on whether the entire sample is known yet. Please note in the Comment field that you are working with an existing dataset. For additional guidance on working with existing datasets see: http://grants.nih.gov/grants/funding/women_min/women_min.htm.

Research Conducted with Foreign Participants

If proposed studies involve foreign participants, investigators are encouraged to design culturally sensitive and appropriate data collection instruments that allow research participants to self-identify their racial and/or ethnic affiliation. However when reporting these data to NIH, these items should be designed in a way that they can be aggregated by the investigator into the OMB-required categories which are defined in Section 5.8,. Also, the investigator can report on any racial or ethnic subpopulations or culturally relevant descriptors by listing this information in the comments section of the Planned Enrollment Report(s). This may be particularly useful when distinctive subpopulations are relevant to the scientific hypotheses being studied. Also, as previously instructed, foreign and domestic subjects must be provided on separate Planned Enrollment Report(s) even if part of the same study.

Delayed-Onset Human Subjects Research

If the proposed research includes studies that meet the definition for delayed-onset human subjects research described in Section 2, Scenario D in the Human Subjects section of the instructions, and it is not possible to describe the proposed study and provide planned enrollment on sex/gender, race, and ethnicity, then enter a comment on the Planned Enrollment Report(s) indicating this is a delayed-onset study. For study title, you may enter the Project Title along with the words “Delayed Onset Study.” If

you expect that more than one study will be delayed onset, it is acceptable to provide only one Planned Enrollment Report indicating delayed onset, but you may wish to indicate in the comments section of the Planned Enrollment Report that more than one study is anticipated under this scenario.

4.4 Inclusion of Children

Create a section entitled "Inclusion of Children" and place it immediately following the section on the Inclusion of Women and Minorities. Although no specific page limits apply to this section of the application, be succinct. The NIH Policy on Inclusion of Children is referenced and described in Section 5.8. For the purpose of implementing these guidelines, a *child* is now defined as an individual under the age of 18 years (for additional information see http://grants.nih.gov/grants/funding/children/children.htm).

Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the age-appropriate inclusion or exclusion of children in the proposed research project. This section is required for all studies meeting the NIH definition for clinical research, not just clinical trials. It is important to provide a detailed plan of who will be included (and/or excluded) based on age. Details about why the individuals in the given age/age range are the appropriate individuals to accomplish the scientific goals of the study should be provided.

Instructions for this item of the Research Plan **including addressing the following points**:

- Describe the age(s) or age range of all individuals to be included in the proposed study.
- Specifically discuss whether children under the age of 18 (as a whole or a subset of individuals under 18) will be included or excluded.
- The description of the plan should include a rationale for selecting a specific age range of children.
- The plan also must include a description of the expertise of the investigative team for working with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.
- When children are involved in research, the Additional Protections for Children Involved as Subjects in Research (45 CFR part 46 Subpart D) apply and must be addressed under the Protections Against Risk subheading (4.1.2.b).

Justifications for Exclusion of Children

For the purposes of this policy, individuals under 18 are defined as a child; however, exclusion of any specific age or age range group should be justified in this section. It is expected that children will be included in all NIH-defined clinical research unless one or more of the following exclusionary circumstances apply:

- The research topic to be studied is not relevant to children.
- Laws or regulations bar the inclusion of children in the research.
- The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be needlessly redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.
- A separate, age-specific study in children is warranted and preferable. Examples include:
    - The condition is relatively rare in children, as compared to adults (in that extraordinary effort would be needed to include children, although in rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected to assemble a similar child population with the rare condition); or

- The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
- Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some instances, consideration should be given to taking these differences into account in the study design and expanding the hypotheses tested, or the interventions planned, to allow inclusion of children rather than excluding them.

- Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). Although children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.
- Study designs are aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children).
- Other special cases can be justified by the investigator and assessed by the review group and the Institute/Center Director to determine if acceptable.

5. Human Subjects Research Policy

Human Subjects Research Policy includes HHS regulations for the protection of human subjects and the following NIH policies related to human subjects research.

5.1 Protection of Human Subjects

The Department of Health and Human Services (HHS) regulations for the Protection of Human Research Subjects provide a systematic means, based on established, internationally recognized ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the HHS. The regulations stipulate that the awardee organization, whether domestic or foreign, bears responsibility for safeguarding the rights and welfare of human subjects in HHS-supported research activities. The regulations require that all organizations engaged in nonexempt human subjects research supported or conducted by the HHS hold a Federalwide Assurance (FWA) with the Office for Human Research Protections (OHRP), and establish appropriate policies and procedures for the protection of human subjects. These regulations, 45 CFR part 46, Protection of Human Subjects, are available from OHRP, Department of Health and Human Services, The Tower Building, 1101 Wootton Parkway, Suite 200, Rockville, MD; telephone: 1-866-447-4777 (toll-free) or (240) 453-6900; e-mail: ohrp@hhs.gov. In general, OHRP considers organizations that receive direct support from HHS for the conduct of nonexempt human subjects research to be engaged in human subjects research. (For more information on whether an institution is engaged in human subjects research, refer to: http://www.hhs.gov/ohrp/policy/engage08.html). When a research project is conducted by multiple organizations, each organization that is engaged in nonexempt human subjects research must hold an FWA and comply with the regulations at 45 CFR 46.

Nonexempt research involving human subjects may only be conducted under an HHS award if the engaged organization(s) is operating in accord with an approved FWA and provides verification that an Institutional Review Board (IRB) that is registered with OHRP has reviewed and approved the proposed activity in accordance with the HHS regulations. No award to an individual will be made unless that individual is affiliated with an assured organization that accepts responsibility for compliance with the HHS regulations. Foreign applicant organizations must also comply with the provisions of the regulations unless a determination of equivalent protections is made in accord with 45 CFR 46.101(h).

Under HHS regulations to protect human subjects, certain research areas are exempt. However, if an applicant makes inappropriate designations of the noninvolvement of human subjects or of exempt categories of research,

this may result in delays in the review of an application or an application not being reviewed. The PHS agency will make a final determination as to whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the Research Plan. With the exception of research projects that meet the criteria for Exemption 4, studies that are exempt from the human subjects regulatory requirements must still address the inclusion of women, minorities, and children in the study design.

Regulations of the Food and Drug Administration (21 CFR 50, 21 CFR 56) generally apply to biomedical research involving an unapproved drug, device or biologic and may apply to certain studies of approved products. Additional information on FDA regulations is available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm. If work falls under FDA's regulatory requirements, the grantee must follow both HHS and FDA human subject protection regulations.

The *National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)* apply to all projects (NIH-funded and non NIH-funded) involving recombinant DNA molecules that are conducted at or sponsored by an institution that receives NIH support for recombinant DNA research. See Part III, 2.9. Research Involving Recombinant DNA, including Human Gene Transfer Research.

Federal requirements to protect human subjects apply to most research on human specimens (such as cells, blood, and urine), residual diagnostic specimens, and medical information. Research involving existing data, documents, records, pathological specimens, diagnostic specimens, or tissues that are individually identifiable is considered "research involving human subjects." Research involving the use of coded private information or biological specimens may not constitute human subjects research. Refer to the OHRP Guidance on Research Involving Coded Private Information or Biological Specimens to clarify when such research is or is not research involving human subjects: http://www.hhs.gov/ohrp/policy/cdebiol.html. The NIH Office of Extramural Research Human Subjects Web site contains additional information and Frequently Asked Questions to help investigators determine whether research that involves the use of human data or biological specimens is human subjects research, and understand how these federal requirements apply to their research. See: http://grants.nih.gov/grants/policy/hs/index.htm.

The HHS regulations require the NIH to evaluate all applications and proposals involving human subjects (45 CFR part 46.120). This independent evaluation is conducted at the NIH through the peer review system and NIH staff review, and, as required, will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. On the basis of this evaluation, the NIH may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

5.1.1 Research Involving the Use of Newborn Blood Spots

As noted in NIH Guide Notice NOT-OD-15-127, NIH funded research using newborn dried blood spots collected on or after March 18, 2015, is considered to be non-exempt human subjects research, and therefore, must follow the HHS protection of human subjects regulations at 45 CFR part 46.

Grant applications submitted to NIH that will use such materials in research should be designated as non-exempt human subjects research and include a complete human subjects section per these instructions including plans for inclusion on the basis of sex/gender, race, ethnicity, and age.

Such applications that are funded by NIH must comply with all the relevant federal regulatory and NIH policy requirements for human subjects research including the requirement that the awardee institution (and all engaged institutions) have a Federalwide Assurance (FWA) from OHRP and certification of IRB approval of the proposed research.

Parental permission must have been obtained in order to use newborn dried blood spots collected on or after March 18, 2015, in NIH-funded research. Waiver of parental permission for such research is not permitted under this legislation.

NIH recognizes that there is no universal agreement on the optimal timing for collection of parental permission for research purposes. Obtaining permission at the time the dried blood spots are collected may be one option.

Ideally, an educational process could take place prior to the process of obtaining permission, and may be provided prenatally or after the birth of the child.

Section 12 of the Newborn Screening Saves Lives Reauthorization Act of 2014 applies to use of newborn dried blood spots in HHS funded research, as "research" is defined in 45 CFR 46.102 (d). Research funded solely by state or private entities does not constitute "Federally funded research" and is not subject to Section 12 of the new law. Non-identifiable newborn dried blood spots collected prior to March 18, 2015, may continue to be used in NIH-funded research without parental permission, and this activity would continue to be considered research that does not involve human subjects under the current human subjects regulations.

5.2 Vulnerable Populations

Investigators who conduct research involving pregnant women, human fetuses and neonates, prisoners (or subjects who become prisoners after the research has started), or children, must follow the provisions of the regulations in Subparts B, C, and D of 45 CFR part 46, respectively. The subparts describe the additional protections required for conducting research involving these populations. Relevant information may be obtained at the OHRP Web site (http://www.hhs.gov/ohrp/policy/index.html).

Exemptions 1-6 (see Exemptions under Human Subjects Research Definitions and Terms, Part III, 3) do **not** apply to research involving prisoners or subjects who become prisoners (see Subpart C). Although Exemptions 1 and 3-6 apply to research involving children (see Subpart D), Exemption 2 can only be used for research involving educational testing or observations of public behavior when the investigator(s) do not participate in the activities being observed.

5.3 Data and Safety Monitoring Plans for Clinical Trials

For each proposed clinical trial (See definition of "clinical trial" under Part III.3), NIH requires a data and safety monitoring plan that describes oversight and monitoring to ensure the safety of participants and the validity and integrity of the data. The level of monitoring should be commensurate with the risks and the size and complexity of the clinical trial. Prior to the accrual of human subjects, a detailed data and safety monitoring plan must be submitted to the applicant's IRB and to the funding entity for approval. Adverse Events must be reported to the IRB, the NIH funding Institute or Center, and other appropriate offices or agencies. This policy requirement is in addition to any monitoring requirements imposed by 45 CFR part 46.

NIH policy specifically requires the establishment of a Data and Safety Monitoring Board (DSMB) for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally for Phase III clinical trials. A DSMB also may be appropriate for clinical trials if the studies are blinded (masked), employ high-risk interventions, or involve vulnerable populations.

Summary reports of adverse events must be provided to the NIH funding IC, individual IRBs and to the DSMB (if one has been established for the trial) in order for them to address reports related to the site for which they have responsibility. Grantees should address questions on this subject to the NIH Program Official.

Further information concerning these requirements is contained in several NIH Guide for Grants and Contracts notices (http://grants.nih.gov/grants/guide/notice-files/not98-084.html and http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html).

5.4 IRB Approval

NIH does not require certification of IRB approval of the proposed research prior to NIH peer review of an application. See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-031.html.

Following NIH peer review, applicants and their institutions will be notified of the need for review and approval of the proposed research by an IRB that is registered with OHRP. See http://www.hhs.gov/ohrp/ to register an

IRB. Certification of IRB approval must be provided through the eRA Commons Just-in-Time module (Part III, Section 1.7).

Because HHS human subject regulations at 45CFR46.103(f) require that each application for non-exempt HHS-supported human subject research be reviewed and approved by an IRB (see also http://www.hhs.gov/ohrp/policy/aplrev.html) the date of approval of the application must be submitted to NIH. However, the IRB must ensure that any corresponding protocol(s) are consistent with the application, and must maintain documentation of IRB approval of all corresponding protocols, including those reviewed by consortium participants. For multi-site research that is not using a single IRB of record, the primary grantee is expected to collect the certification from each subrecipient.

Awardees involved in multi-site research may agree to rely on a single IRB of record. The IRB of record must have an assurance with OHRP. Following OHRP guidance, NIH expects that such reliance arrangements will be documented through the signing of an IRB Authorization Agreement.

Any modifications to the Research Plan in the application, required by either NIH or by the IRB, must be submitted with follow-up certification of IRB approval to the NIH before the competing award is made. It is the responsibility of the PD/PI and the applicant organization to submit the follow-up documentation.

IRB approval must be dated within the last year to be valid. If more than a year will have elapsed between the initial IRB review date and the anticipated award date, the IC shall require re-review by the IRB prior to award.

Continuing IRB review of ongoing human subjects research is required by 45 CFR part 46. 109(e). A progress report for continuation support should not be submitted until certification of annual IRB review as been obtained. The awardee institution must track and document IRB approval for all components of an award. Although the RPPR does not require submission of a date of IRB approval, progress reports using the PHS 2590 should report the most recent IRB approval date for any component which the IRB has approved

5.5 Required Education in the Protection of Human Research Participants

NIH requires education on the protection of human research participants for all individuals identified in PHS applications as senior/key personnel who will be involved in the design or conduct of human subjects research, before funds are awarded for applications or contract proposals involving human subjects. For information relating to this requirement, see the following notices http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html and http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html, and Frequently Asked Questions at: http://grants.nih.gov/grants/policy/hs_educ_faq.htm. Prior to award, applicants will be required to provide a description of education completed in the protection of human subjects for all senior/key personnel involved in the design or conduct of human subjects research. Although NIH does not endorse specific programs, curricula are available and provide guidance or can be modified to provide training in this area. See http://grants.nih.gov/grants/policy/hs/training.htm for a free tutorial developed by NIH and other resources on human subjects protection training. For information on facilitating education and developing curricula, see http://sigs.nih.gov/bioethics/Pages/default.aspx.

5.6 NIH Policy on the Inclusion of Women and Minorities in Clinical Research

NIH-conducted and –supported clinical research must comply with the NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm), in accord with Public Health Service Act sec. 492B, 42 U.S.C. sec 289a-2.

The NIH policy requires that women and members of minority groups and their subpopulations be included in all NIH-supported biomedical and behavioral research projects involving NIH-defined clinical research unless a clear and compelling rationale and justification establishes to the satisfaction of the funding IC Director that

inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances must be designated by the Director, NIH, upon the recommendation of an IC Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. This policy applies to research subjects of all ages.

The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The Research Plan should describe the composition of the proposed study population in terms of sex/gender, race, and ethnicity, and provide a rationale for selection of subjects. It is important to justify the proposed sample on the basis of sex/gender, race, and ethnicity in the context of the scientific goals of the proposed study(s) with discussion of the demographics of the population under study and/or who is at risk for the disease/condition. Such a plan should contain a description of the proposed outreach programs for recruiting women and minorities as participants. See http://grants.nih.gov/grants/funding/women_min/women_min.htm.

In addition, as detailed in Section 4.2.1 of these instructions, when conducting an NIH-defined Phase III clinical trial, there are additional requirements and considerations related to valid analysis to explore differences on the basis of sex/gender, race, and ethnicity.

5.7 NIH Policy on Reporting Race and Ethnicity Data for: Subjects in Clinical Research

The Office of Management and Budget (OMB) defines minimum standards for maintaining, collecting and presenting data on race and ethnicity for all Federal reporting agencies (including NIH) in OMB Directive 15: http://www.whitehouse.gov/omb/fedreg_1997standards.

The standards were revised in 1997 and include two ethnic categories (Hispanic or Latino and Not Hispanic or Latino) and five racial categories (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White). The categories in this classification are social-political constructs and should not be interpreted as being anthropological in nature. NIH is required to use these definitions to allow comparisons to other federal databases, especially the census and national health databases. Federal agencies will not present data on detailed categories if doing so would compromise data quality or confidentiality standards.

Collection of this information and use of these categories is required for research that meets the NIH definition of clinical research. The collection of greater detail is encouraged, for example on racial or ethnic subpopulations. However, any collection that uses more detail must be designed in a way that data can be aggregated into these minimally required OMB categories. Use self-report or self-identification to collect this information from subjects by asking two separate questions – one on ethnicity and one on race. Collect ethnicity information first, followed by the question on race and provide participants with the option to select more than one racial category. Participants also have the option not to identify. When feasible, NIH encourages investigators to include information about individuals who select more than one racial category and consider that data in their analyses. Participants who self-identify with more than one racial category should be reported to the NIH under the "More than one race" category of the report. See NIH Policy on Inclusion of Women and Minorities and http://grants.nih.gov/grants/funding/women_min/women_min.htm.

The following definitions apply to the minimum standards for the ethnic and racial categories.

Ethnic Categories:

Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish origin," can be used in addition to "Hispanic or Latino."

Not Hispanic or Latino

Racial Categories:

American Indian or Alaska Native: A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.

Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)

Black or African American: A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

Native Hawaiian or Other Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Ethnic/Racial Subpopulations: In addition to OMB ethnic and racial categories, each ethnic/racial group contains subpopulations that are delimited by geographic origins, national origins, and/or cultural differences. It is recognized that there are different ways of defining and reporting racial and ethnic subpopulation data. The subpopulation to which an individual is assigned depends on self-reporting of specific origins and/or cultural heritage. Attention to subpopulations also applies to individuals who self-identify with more than one race. These ethnic/racial combinations may have biomedical, behavioral, and/or socio-cultural implications related to the scientific question under study.

5.8 NIH Policy on Inclusion of Children

Research involving children (see definition of "child") must comply with the NIH Policy and Guidelines on the Inclusion of Children in Clinical Research. Investigators should obtain full copies of the Policy and Guidelines from NIH staff, or from http://grants.nih.gov/grants/funding/children/children.htm.

NIH policy requires that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH unless there are clear and compelling reasons not to include them. Therefore, applications proposing clinical research must include a description of plans for including children. If children (or a subset of children) will be excluded from the research, the application must include an acceptable justification for the exclusion. For additional details and guidance, please refer to Part II, Section 4.4 of these instructions as well as http://grants.nih.gov/grants/funding/children/children.htm.

The involvement of children as subjects in research must be in compliance with all applicable subparts of 45 CFR part 46 as well as with other pertinent Federal laws and regulations.

IRBs have special review requirements to protect the well-being of children who participate in research. These requirements relate to risk, benefit, parental/guardian consent, and assent by children, and to research involving children who are wards of the state or of another institution. The local IRB approves research that satisfies the conditions set forth in the regulations.

5.9 Research on Transplantation of Human Fetal Tissue

In signing the application Face Page or checking the "I agree" box on line 17 of the SF 424 (R&R) Cover Form, the Authorized Organization Representative of the applicant organization certifies that if research on the transplantation of human fetal tissue is conducted, the applicant organization will make available, for audit by the Secretary, HHS, the physician statements and informed consents required by section 498A (b)(2) and (c) of the Public Health Service Act, 42 U.S.C. 289g (b)(2) and (c), or ensure HHS access to those records, if maintained by an entity other than the applicant organization.

5.10 Research Using Human Embryonic Stem Cells

In signing the application Face Page or checking the "I agree" box on line 17 of the SF 424 (R&R) Cover Form, the Authorized Organization Representative of the applicant organization certifies that if research using human embryonic stem cells is proposed, the applicant organization will identify hESCs to be used from the NIH Registry (http://stemcells.nih.gov/research/registry/), or, if a specific cell line cannot be referenced at the time of application, certify that one from the NIH Registry will be used, in accord with the NIH Guidelines on Human Stem Cell Research (http://stemcells.nih.gov/policy/2009guidelines.aspx). The AOR further certifies that the hESCs will be used in accordance with any restrictions associated with the line as cited on the Registry (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-029.html). See http://stemcells.nih.gov/info/Pages/default.asp for additional information on stem cells, Federal policy statements, and guidelines on federally funded stem cell research.

5.11 ClinicalTrials.gov Requirements

In signing the application Face Page or checking the "I agree" box on line 17 of the SF424 (R&R) Cover Form, the Authorized Organization Representative of the applicant organization certifies that if the research is an applicable clinical trial under Public Law 110-85, the applicant organization will be in compliance with the registration and reporting requirements of Public Law 110-85 (Section 4.1.6).

PART III

Policies, Assurances, Definitions, and Other Information

1. Policy

1.1 Applications That Include Consortium/Contractual Facilities and Administrative Costs

See: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-004.html.

NIH policy provides for exclusion of consortium/contractual F&A when determining if an applicant is in compliance with a direct cost limitation. This policy extends to all applications involving consortium/contractual facilities and administrative (F&A) costs, regardless of budget amount or budget format (e.g., modular and non-modular). (See also Notice OD-04-040.)

This policy applies to all solicited and investigator-initiated applications and to all active announcements (Request for Applications and Program Announcements), regardless of the announcement issue date.

This policy is particularly relevant to all applications that include a limitation on direct costs. While consortium F&A costs will continue to be requested and awarded, applicants should separate these costs when determining if a budget exceeds a direct cost limit.

This policy impacts eligibility to submit a modular budget. The modular budget format is used for applications requesting $250,000 or less in direct costs per year. Consortium/contractual F&A costs are not factored into this direct cost limit and may be requested in addition to the $250,000.

The policy also impacts applications requesting a budget of $500,000 direct costs or more for any year. These applications require prior approval from Institute/Center staff; however, the limit is exclusive of any consortium F&A costs.

The implications of this policy do not affect the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs since the statutory budget guidelines are based on total costs, not direct costs.

1.2 Resubmission of Unfunded RFA Applications

The majority of grant applications submitted to NIH each year are investigator-initiated. However, the Institutes and Centers of NIH also solicit grant applications on specific topics through the use of Requests for Applications (RFAs). This policy applies to all activity codes that might be solicited via an RFA and to instances where there is a change in activity code. Unless otherwise noted in a particular FOA, unfunded applications should be submitted as **new** applications if the grant applications fall into the following categories:

1. Applications that were originally submitted in response to an RFA and then resubmitted as an investigator-initiated application.
2. Applications that were originally submitted as investigator-initiated applications and subsequently resubmitted in response to an RFA.
3. Applications that were originally submitted using one grant activity code and subsequently resubmitted using a different activity code (for example, an application that was originally an R01 and is resubmitted as an R21).

Since an RFA often has special considerations of eligibility, scientific scope, and review criteria, unfunded RFA applications must be resubmitted as **new** applications to another FOA. Similarly, a change of activity code (e.g., from an R01 to an R21, or from an R03 to an R01) usually involves a change of eligibility criteria, application characteristics, dollar limits, or time limits. This also suggests that consideration as a new application is the most appropriate course. Because the application will be new it will be easier to conform to the new application requirements, which should be an advantage to the applicant in the review process. Additionally, submission of

a new application will allow the applicant to benefit fully from the NIH policy that allows an applicant one resubmission (see http://grants.nih.gov/grants/policy/amendedapps.htm).

NEW APPLICATIONS: The new application must be submitted on the scheduled due dates for new applications (see http://grants.nih.gov/grants/funding/submissionschedule.htm). Do **not** include an Introduction describing the changes and improvements made and do **not** mark text to indicate the changes. Although the investigator may still benefit from the previous review, the applicant should not explicitly address reviewers' comments. The reviewers will not be provided with the previous Summary Statement. The investigator will be allowed to submit the new application and one resubmission of the application, should that be necessary.

1.3 NIH Policy on Resubmission Applications

See: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-140.html,
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-080.html,
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-016.html, and
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-003.html.

For all original new (i.e., never submitted) and competing renewal applications, NIH will accept only a single amendment (A1) to the original application. A lengthy hiatus after the initial submission may be marked by significant advances in the scientific field and the comments of the reviewers may no longer be relevant. Therefore, a resubmission application must be submitted within 37 months after the date of receipt ("receipt date") of the initial New, Renewal, or Revision application (see NOT-OD-10-140). After 37 months, you may submit a New application. Any second resubmission will be administratively withdrawn and not accepted for review.

In the referral process, NIH staff look at all aspects of the application, not just the title and description (abstract). Requesting review by a different review committee does not affect the implementation of this policy. When necessary, previous applications are analyzed for similarities to the present one. Thus, identical applications or those with only minor changes will not be accepted for review.

1.4 Policy on the Acceptance for Review of Unsolicited Applications That Request $500,000 or More in Direct Costs

Applicants must seek agreement to accept assignment from Institute/Center staff at least six weeks prior to the anticipated submission of any application requesting $500,000 or more in direct costs for any year. For the purposes of this policy, the $500,000 limit excludes any consortium F&A costs.

See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-004.html.

The NIH supports research projects with large budgets but needs to consider such awards as early as possible in the budget and program planning process. Regardless of the merit of the application or the budget justification, unanticipated requests for unusually high amounts of direct costs are difficult for NIH to manage. It is in the best interest of all parties if applicants anticipating large direct costs contact the appropriate NIH program staff as early as possible to ensure that an Institute/Center (IC) would be willing to accept the application. If staff is contacted less than six weeks before submission, there may be insufficient time to make a determination about assignment prior to the intended submission date. If the requested dollars are significantly greater than $500,000, then approval should be sought even earlier.

This prior acceptance policy does not apply to applications submitted in response to RFAs or in response to other Announcements that include specific budgetary limits. Such applications must be responsive to any budgetary limits specified; however, any specified budgetary limit excludes consortium F&A costs.

PROCEDURES

- An applicant planning to submit a grant application with $500,000 or more in direct costs for any year (excluding consortium F&A costs) is required to contact in writing or by telephone NIH IC program staff. This contact should be made during the development process of the application but no later than six weeks before the anticipated submission date. If the IC is willing to accept assignment of the application for consideration of funding, the staff will notify the Center for Scientific Review before the application is submitted.
- The PD/PI must include a cover letter with the application. That cover letter must identify the program staff member contacted and the Institute/Center that has agreed to accept assignment of the application.
- An application received without indication of prior staff concurrence and identification of program staff contacted will not be reviewed. Therefore, NIH strongly encourages applicants to contact appropriate IC staff at the earliest possible time.

For additional information about this policy, contact the program staff at any Institute/Center. Applicants who are uncertain about which IC may have the greatest interest in the research for which support is sought should contact the NIH CSR Receipt and Referral Office at (301) 435-0715.

SBIR/STTR applicants are NOT required to obtain pre-approval to submit an application if the budget exceeds $500K in direct costs per year. The $500K Policy does not apply to applications submitted in response to RFAs or other solicited applications, and SBIR/STTRs are solicited applications. In addition, the budget levels set for SBIR/STTRs are statutory guidelines, not caps.

However, SBIR/STTR applicants are strongly encouraged to contact Institute/Center Program Staff before submitting an application in which the budget and/or project period deviates from the statutory guidelines. While the Phase I and Phase II award levels are guidelines that allow for applicants to propose a budget and project period appropriate for completion of the research project, deviations from the guidelines should be discussed with appropriate NIH staff listed in the Awarding Component/Agency Contact Information Table prior to submission of the application.

1.5 Sharing Research Resources

Investigators conducting biomedical research frequently develop unique research resources. NIH considers the sharing of such unique research resources (also called research tools) an important means to enhance the value of NIH-sponsored research. Restricting the availability of unique resources can impede the advancement of further research. Therefore, when these resources are developed with NIH funds and the associated research findings have been published or after they have been provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. At the same time NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with federal funding pursuant to the Bayh Dole Act. See the NIH Grants Policy Statement, and the Office of Extramural Research, Division of Extramural Inventions & Technology Resources (DEITR), Intellectual Property Policy page: http://inventions.nih.gov.

The adequacy of resource sharing plans is considered by reviewers when a competing application is evaluated. Reviewers are asked to describe their assessment of the sharing plan(s) in an administrative note, and will not normally include their assessment in the overall impact/priority score. Program staff are responsible for overseeing resource sharing policies and for assessing the appropriateness and adequacy of any proposed resource sharing plans.

1.5.1 Data Sharing Policy

All investigator-initiated applications with direct costs of $500,000 or greater (exclusive of consortium F&A) in any single year are expected to address data-sharing in their application. Applicants are encouraged to discuss data-sharing plans with their program contact at the time they negotiate an agreement with the Institute/Center (IC) staff to accept assignment of their application as described at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html.

Applicants are reminded that agreement to accept assignment of applications $500,000 or greater must be obtained at least six weeks in advance of the anticipated submission date. Instructions related to the data-sharing policy as it is applied to applications and proposals responding to a specific Request for Application (RFA) or Request for Proposals (RFP) will be described in the specific solicitation. In some cases, other Funding Opportunity Announcements (FOAs) may request data-sharing plans for applications that are less than $500,000 direct costs in any single year.

NIH recognizes that in some cases data-sharing may be complicated or limited by institutional policies, local IRB rules, as well as local, state and Federal laws and regulations, including the HIPAA Privacy Rule. The rights and privacy of individuals who participate in NIH-sponsored research must be protected at all times. Thus, data intended for broader use should be free of identifiers that would permit linkages to individual research participants and variables that could lead to deductive disclosure of the identity of individual subjects. When data-sharing is limited, applicants should explain such limitations in their data-sharing plans.

For SBIR grantees only, under the Small Business Act, SBIR grantees may withhold their data for 4 years after the end of the award. The Small Business Act provides authority for NIH to protect from disclosure and nongovernmental use all SBIR data developed from work performed under an SBIR funding agreement for a period of 4 years after the closeout of either a Phase I or Phase II grant unless NIH obtains permission from the awardee to disclose these data. The data rights protection period lapses only upon expiration of the protection period applicable to the SBIR award, or by agreement between the small business concern and NIH.

For more information on data-sharing, please see: http://grants.nih.gov/grants/ policy/data_sharing/ and the NIH Final Policy on Sharing Research Data.

1.5.2 Sharing Model Organism Policy

All applications where the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding so that other researchers can benefit from these resources, or state appropriate reasons why such sharing is restricted or not possible. Model organisms include but are not restricted to mammalian models, such as the mouse and rat; and non-mammalian models, such as budding yeast, social amoebae, round worm, fruit fly, zebra fish, and frog. Research resources to be shared include genetically modified or mutant organisms, sperm, embryos, protocols for genetic and phenotypic screens, mutagenesis protocols, and genetic and phenotypic data for all mutant strains.

This expectation is for **all** applications where the development of model organisms is anticipated, regardless of funding amount.

For additional information on this policy, see the NIH Model Organism for Biomedical Research Web site at: http://www.nih.gov/science/models/ and NIH Guide Notices OD-04-042: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html, and OD-04-066: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-066.html.

1.5.3 NIH Genomic Data Sharing (GDS) Policy

All applications, regardless of the funding amount requested, proposing to generate large-scale human or non-human genomic data (e.g., genome-wide association studies (GWAS), single nucleotide polymorphism (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data) are expected to provide a genomic data sharing plan. Investigator and institution responsibilities for data submission and access are governed by the NIH (GDS Policy, NIH Guide NOT-OD-14-124). Supplemental Information to the Genomic Data Sharing Policy provides examples of genomic research projects that are subject to the policy. Investigators proposing to generate large-scale human genomic data from samples, clinical specimens or cell lines collected after January 25, 2015, are expected to have consent for the use and sharing of genomic and phenotypic data for future research purposes and to be shared broadly, even if the specimens or cell lines are de-identified. Applicants may request exceptions to the NIH consent expectations for compelling scientific reasons in the funding application. For additional information see the GDS website at http://gds.nih.gov/.

In addition to the information detailed above, grantees are required to submit an Institutional Certification as part of the Just in Time process (see 1.7 Just-in-Time Policy).

1.6 Inventions and Patents

NIH Grants Policy and Federal law require NIH recipient organizations to promptly report all inventions that are either conceived or first actually reduced to practice using NIH funding. Invention reporting compliance is described at http://www.iedison.gov. Grantees are encouraged to submit reports electronically using Interagency Edison (http://www.iedison.gov). Information from these reports is retained by the NIH as confidential and submission does not constitute any public disclosure. Failure to report as described at 37 CFR Section 401.14 is a violation of 35 U.S.C. 202 and may result in loss of the rights of the recipient organization. Inquiries or correspondence should be directed to **Division of Extramural Inventions and Technology Resources, Office of Policy for Extramural Research Administration, OER, NIH, 6705 Rockledge Dr., Suite 310, MSC 7980, Bethesda, MD 20892-7980, Telephone: (301) 435-1986.**

1.7 Just-In-Time Policy

These procedures allow certain elements of an application to be submitted later in the application process, after review when the application is under consideration for funding. The standard application elements are listed. Other program-specific information may also be requested using this procedure. (Applications in response to RFAs also may be subject to these procedures. The RFA will specify the timing and nature of required submissions.)

The information eligible for Just-in-Time submission includes:

- Current Other Support (not generally required for Fellowship applicants): See Section 1.8 Other Support policy information below. Use the sample format provided on the Other Support Format Page (MS WORD or PDF). For all senior/key personnel, provide details on adjustment of any budgetary, scientific, or effort overlap if the application is funded.

  For Career Development Award applicants, information on all active support for the candidate, mentor(s), co-mentor(s), and senior/key personnel may be requested by the awarding component prior to award.

- Certifications:
  - ***Certification of IRB Approval***. If the proposed project involves human subjects research, the certification date of IRB review and approval must be submitted. Pending, conditional, or out-of-date approvals are not acceptable. See Part II.5.4 IRB Approval.
  - ***Verification of IACUC Approval***. If the proposed project involves research with live vertebrate animals, provide the Animal Welfare Assurance number of the applicant organization (if not previously provided), date of IACUC approval of the research proposed in the application, and any IACUC-imposed changes. Pending or out-of-date approvals cannot be accepted. IACUC approval must have been granted within three years to be valid. See 2.2 Vertebrate Animals.
  - ***Human Embryonic Stem Cells (hESCs)***. If the proposed project involves hESCs and the applicant did not identify a hESC line from the NIH Human Embryonic Stem Cell Registry in the application, the line(s) may be submitted as an "Other Upload" file.
  - ***Human Subjects Education Requirement.*** If the proposed project involves human subjects research, certification that each person identified as senior/key personnel involved in the design or conduct of research involving human subjects has completed an educational program in the protection of human subjects must be submitted. See Required Education in the Protection of Human Research Participants in Part II, 5.5.

- ***Institutional Certification for Human Genomic Data Sharing***. If the proposed project involves a genomic data sharing plan for the generation of human genomic data, investigators must submit an Institutional Certification, or, in some cases, a Provisional Institutional Certification. Institutional certification forms and directions for completing them are available on the NIH GDS: http://gds.nih.gov/Institutional_Certifications.html. This certification should be submitted as an "Other Upload" in the eRA Commons Just-in-Time module.
- ***SBIR Funding Agreement Certification***. For SBIR applicants, provide only upon request the SBIR Funding Agreement Certification described in Section 2.18. This certification is available in fillable format on the SBIR/Forms website: http://grants.nih.gov/grants/forms.htm#sbir. This should be submitted as an "Other Upload" in the eRA Commons Just-in-Time module.
- ***STTR Funding Agreement Certification***. For STTR applicants, provide only upon request the STTR Funding Agreement Certification described in Section 2.19. This certification is available in fillable format on the SBIR/Forms website: http://grants.nih.gov/grants/forms.htm#sbir. This should be submitted as an "Other Upload" in the eRA Commons Just-in-Time module.

- Other Information Requested by the Awarding IC: Additional JIT information (i.e., revised budgets, changes to the human subjects, or vertebrate animal sections of the application) may be requested by NIH Institutes and/or Centers on a case-by-case basis. These should be submitted as an "Other Upload" file.

Applicants will be notified (primarily by e-mail) when Just-in-Time information is needed. This notification is not a Notice of Award nor should it be construed to be an indicator of possible funding. Applicants should only submit this information when requested. In some circumstances the GMO may ask for information in addition to the descriptions above. Information must be submitted electronically using the Just-in-Time feature in the eRA Commons. For information on the Commons see: https://commons.era.nih.gov/ commons/index.jsp.

The requirement for applicants to verify the accuracy and validity of all administrative, fiscal, and programmatic information extends to information submitted through the Just-in-Time process. Applicants are responsible for promptly notifying NIH of any substantive changes to previously submitted Just-in-Time information up to the time of award. This includes items such as Other Support changes that could lead to budgetary overlap, scientific overlap, or commitment of effort greater than 12 person-months for the PD/PI(s) or any Senior/Key Personnel; or any changes in the use or approval of vertebrate animals or human subjects. Similar to the NIH public policy requirements, applicants are responsible for establishing and maintaining the necessary processes to monitor its compliance and informing NIH of any problems or concerns. Failure to address changes to Just-in-Time submissions prior to award does not diminish the applicant's responsibility to address changes post-award by submitting a prior approval request to NIH.

1.8 Other Support

Do not submit information on Other Support with the application beyond that required in the biographical sketch. See 1.7 Just-in-Time Policy.

Information on Other Support is required for all applications that are to receive grant awards, except Program Directors, training faculty and other individuals involved in the oversight of training grants. NIH will request complete and up to date information from applicants at an appropriate time *after peer review*. The Institute/Center scientific program and grants management staff will review this information prior to award.

Do not confuse Research Support with Other Support, they are distinctly different. As part of the biosketch section of the application, Research Support highlights your accomplishments, and those of your colleagues, as scientists. This information will be used by the reviewers in the assessment of each individual's qualifications for a specific role in the proposed project, as well as to evaluate the overall qualification of the research team. In

contrast, Other Support information is required for all applications that are selected to receive grant awards and includes detailed financial information. NIH staff will request complete and up-to-date "Other Support" information *after* peer review. This information will be used to check that the proposed research is not already funded through other sources.

Information on Other Support is also required in the progress report for all senior/key personnel, excluding consultants, when there has been a change in active other support. Other Support is not required in progress reports for Program Directors, training faculty, and other individuals involved in the oversight of training grants.

Other Support Policy

Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards. Training awards, prizes, or gifts are not included.

Information on Other Support assists awarding agency staff in the identification and resolution of potential overlap of support. Overlap, whether scientific, budgetary, or commitment of an individual's effort greater than 100 percent (i.e., 12 person months), is not permitted. The goals in identifying and eliminating overlap are to ensure that sufficient and appropriate levels of effort are committed to the project; that there is no duplication of funding for scientific aims, specific budgetary items, or an individual's level of effort; and that only funds necessary to the conduct of the approved project are included in the award.

Budgetary overlap occurs when duplicate or equivalent budgetary items (e.g., equipment, salary) are requested in an application but are already provided for by another source.

Commitment overlap occurs when a person's time commitment exceeds 100 percent (i.e., 12 person months), whether or not salary support is requested in the application. While information on other support is only requested for senior/key personnel (excluding consultants), no individuals on the project may have commitments in excess of 100 percent or 12 person months.

Scientific overlap occurs when: (1) substantially the same research is proposed in more than one application or is submitted to two or more different funding sources for review and funding consideration, or (2) a specific research objective and the research design for accomplishing that objective are the same or closely related in two or more applications or awards, regardless of the funding source. Potential scientific overlap is to be addressed by the SRG *only* by its identification in an Administrative Note in the Summary Statement.

Resolution of Overlap. Resolution of overlap occurs at the time of award in conjunction with applicant institution officials, the PD/PI, and awarding agency staff.

Other Support Information

Information on Other Support for competing applications should be submitted ONLY when requested by the NIH Institute/Center (IC).

There is no form page for Other Support. Follow the sample format provided below. The sample is intended to provide guidance regarding the type and extent of information requested.

Follow the instructions below to complete the other support:

- **Other Support for Competing Applications:** Information on active and pending Other Support is required for senior/key personnel, excluding consultants. For individuals with no active or pending support, indicate "None." Neither the application under consideration nor the current PHS award for this project should be listed as Other Support. Do not include Other Support for individuals listed as "Other Significant Contributors" unless their involvement has changed so that they now meet the definition of "senior/key personnel." If the support is provided under a consortium/contractual arrangement or is part of a multiproject award, indicate the project number, PD/PI, and source for the overall project, and provide all other information for the subproject only.

- **Other Support for Progress Reports:** Information should be submitted only for the PD/PI and for those individuals considered by the grantee to be key to the project when there has been a change in active other support. Indicate what the change has been. List the award for which the progress report is being submitted and include the effort that will be devoted in the next reporting period. Do not include Other Support for individuals listed as "Other Significant Contributors" unless their involvement has changed so that they now meet the definition of "senior/key personnel." Submission of other support information is not necessary if support is pending or for changes in the level of effort for active support reported previously.

Instructions for Selected Items

Project Number: If applicable, include a code or identifier for the project.

Source: Identify the agency, institute, foundation, or other organization that is providing the support. Include institutional, federal, public, and private sources of support.

Major Goals: Provide a brief statement of the overall objectives of the project, subproject, or consortium/contractual arrangement.

Dates of Approved/Proposed Project: Indicate the inclusive dates of the project as approved/proposed. For example, in the case of NIH support, provide the dates of the approved/proposed competitive segment.

Annual Direct Costs: In the case of an active project, provide the current year's direct cost budget. For a pending project, provide the proposed direct cost budget for the initial budget period.

Percent Effort/Person Months: For an active project, provide the level of actual effort in person months (even if unsalaried) for the current budget period. Person months should be classified as academic, calendar and/or summer. For a pending project, indicate the level of effort in person months as proposed for the initial budget period. In cases where an individual's appointment is divided into academic and summer segments, indicate the proportion of each devoted to the project.

Overlap: After listing all support, summarize for each individual any potential overlap with the active or pending projects and this application in terms of the science, budget, or an individual's committed effort.

Sample Format for Other Support for Competing Applications

OMB No. 0925-0001 (Rev. 06/15 Approved Through 10/31/2018)

For New and Renewal Applications (PHS 398) – DO NOT SUBMIT UNLESS REQUESTED

PHS 398 OTHER SUPPORT

Provide active and pending support for all senior/key personnel. **Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards.** Training awards, prizes, or gifts do not need to be included.

There is no "form page" for other support. Information on other support should be provided in the *format* shown below, using continuation pages as necessary. The sample below is intended to provide guidance regarding the type and extent of information requested.
For instructions and information pertaining to the use of and policy for other support, see Other Support in the Supplemental Instructions, Part III, Policies, Assurances, Definitions, and Other Information.
Effort devoted to projects must be measured using person months. Indicate calendar, academic, and/or summer months associated with each project.

Format

NAME OF INDIVIDUAL ACTIVE/PENDING		
Project Number (Principal Investigator) Source Title of Project *(or Subproject)* The major goals of this project are…	Dates of Approved/Proposed Project Annual Direct Costs	Person Months (Cal/Academic/ Summer)

OVERLAP *(summarized for each individual)*

Samples

ANDERSON, R.R.

ACTIVE

2 R01 HL 00000-13 (Anderson) — 3/1/2012 – 2/28/2017 — 3.60 calendar
NIH/NHLBI — $186,529
Chloride and Sodium Transport in Airway Epithelial Cells

The major goals of this project are to define the biochemistry of chloride and sodium transport in airway epithelial cells and clone the gene(s) involved in transport.

5 R01 HL 00000-07 (Baker) — 4/1/2001 – 3/31/2012 — 1.20 calendar
NIH/NHLBI — $122,717
Ion Transport in Lungs

The major goal of this project is to study chloride and sodium transport in normal and diseased lungs.

R000 (Anderson) — 9/1/2014 – 8/31/2017 — 1.20 calendar
Cystic Fibrosis Foundation — $43,123
Gene Transfer of CFTR to the Airway Epithelium

The major goals of this project are to identify and isolate airway epithelium progenitor cells and express human CFTR in airway epithelial cells.

PENDING

DCB 950000 (Anderson) — 12/1/2014 – 11/30/2016 — 2.40 calendar
National Science Foundation — $82,163
Liposome Membrane Composition and Function

The major goals of this project are to define biochemical properties of liposome membrane components and maximize liposome uptake into cells.

Page ____ **Other Support Format Page**

OVERLAP

There is scientific overlap between aim 2 of NSF DCB 950000 and aim 4 of the application under consideration. If both are funded, the budgets will be adjusted appropriately in conjunction with agency staff.

RICHARDS, L.

NONE

HERNANDEZ, M.

ACTIVE

5 R01 CA 00000-07 (Hernandez)	4/1/2010 – 3/31/2017	3.60 academic
NIH/NCI	$110,532	
Gene Therapy for Small Cell Lung Carcinoma		

The major goals of this project are to use viral strategies to express the normal p53 gene in human SCLC cell lines and to study the effect on growth and invasiveness of the lines.

5 P01 CA 00000-03 (Chen)	7/1/2014 – 6/30/2016	1.80 academic
NIH/NCI	$104,428 (sub only)	3.00 summer
Mutations in p53 in Progression of Small Cell Lung Carcinoma		

The major goals of this subproject are to define the p53 mutations in SCLC and their contribution to tumor progression and metastasis.

BE 00000 (Hernandez)	9/1/2014 – 8/31/2017	1.80 academic
American Cancer Society	$86,732	
p53 Mutations in Breast Cancer		

The major goals of this project are to define the spectrum of p53 mutations in human breast cancer samples and correlate the results with clinical outcome.

OVERLAP

Potential commitment overlap for Dr. Hernandez between 5 R01 CA 00000-07 and the application under consideration. If the application under consideration is funded with Dr. Hernandez committed at 3.60 person months, Dr. Hernandez will request approval to reduce her months on the NCI grant.

BENNETT, P.

ACTIVE

Investigator Award (Bennett)	9/1/2015 – 8/31/2017	9.00 calendar
Howard Hughes Medical Institute	$581,317	
Gene Cloning and Targeting for Neurological Disease Genes		

This award supports the PI's program to map and clone the gene(s) implicated in the development of Alzheimer's disease and to target expression of the cloned gene(s) to relevant cells.

OVERLAP: None

Sample Format for Other Support for Progress Reports

OMB No. 0925-0002 (Rev. 06/15 Approved Through 10/31/2018)

PHS 2590/RPPR OTHER SUPPORT FORMAT PAGE

Submit other support for all new senior/key personnel, and updated other support for all senior/key personnel for whom there has been a change since the last reporting period.

Provide only active support for all new senior/key personnel. Provide updated other supported for all senior/key personnel for whom there has been a change in other support. If a previously active grant has terminated and/or if a previously pending grant is now active, update by annotating accordingly.

Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards. Training awards, prizes, or gifts do not need to be included. Effort devoted to projects must be reported in person months; indicate calendar, academic, and/or summer months associated with each project.

Use the suggested format shown below and continuation pages as necessary. The sample format below provides guidance regarding the type and extent of information that should be provided.

Format

NAME OF INDIVIDUAL ACTIVE/INACTIVE		
Project Number or Name (PD/PI name) Source of Support Title of Project or Subproject The major goals of this project are…	Dates of Approved/Proposed Project Annual Direct Costs	Person Months (Calendar/Academic/ Summer)
OVERLAP *(summarized for each individual)*		

Examples

NEW SENIOR/KEY PERSONNEL (D.2.b)

BENNETT, P.
ACTIVE

Investigator Award (Bennett) 9/1/2015 – 8/31/2020 6.0 calendar
Howard Hughes Medical Institute $581,317
Gene Cloning and Targeting for Neurological Disease Genes
This award supports the PI's program to map and clone the gene(s) implicated in the development of Alzheimer's disease and to target expression of the cloned gene(s) to relevant cells.

5 R01 HG 000000-07 (Daumier) 3/1/2009 – 2/28/2018 3.6 calendar
NIH/NHGRI $196,639
Identification of the Risk Factor Genes for Alzheimer's Disease

The major goals of this project are to identify of new Alzheimer's disease genes and predicting Alzheimer's disease.

(THIS AWARD)
2 R01 HL 000000-14 (Anderson) 3/1/2002 – 2/28/2017 1.2 calendar
NIH/NHLBI $186,529
Chloride and Sodium Transport in Airway Epithelial Cells

OVERLAP No Overlap

RICHARDS, L.
No Other Support

Page ___ **Other Support Format Page**

OMB No. 0925-0002 (Rev. 06/15 Approved Through 10/31/2018)

CHANGES IN OTHER SUPPORT (D.2.c)

ANDERSON, R.R.

ACTIVE

(THIS AWARD)

2 R01 HL 000000-14 (Anderson)	3/1/2002 – 2/28/2017	3.6 calendar
NIH/NHLBI	$186,529	
Chloride and Sodium Transport in Airway Epithelial Cells		

The major goals of this project are to define the biochemistry of chloride and sodium transport in airway epithelial cells and clone the gene(s) involved in transport.

5 R01 HL 00000-04 (Baker)	4/1/2012 – 3/31/2016	1.2 calendar
NIH/NHLBI	$122,717	
Ion Transport in Lungs		

The major goal of this project is to study chloride and sodium transport in normal and diseased lungs.

R000 (Anderson)	9/1/2001 – 8/31/2016	1.2 calendar
Cystic Fibrosis Foundation	$43,123	
Gene Transfer of CFTR to the Airway Epithelium		

The major goals of this project are to identify and isolate airway epithelium progenitor cells and express human CFTR in airway epithelial cells.

(NEW)

R01 DK000000-01 (Zimmerman)	9/1/2015 – 8/31/2019	1.2 calendar
NIH/NIDDK	$187,265	
Cystic Fibrosis Related Diabetes and Lung Function		

The major goals of this project are to determine how CFRD contributes to lung function decline.

OVERLAP No Overlap

INACTIVE

DCB 950000 (Anderson)	12/1/2008 – 11/30/2011	2.4 calendar
National Science Foundation	$82,163	
Liposome Membrane Composition and Function		

The major goals of this project are to define biochemical properties of liposome membrane components and maximize liposome uptake into cells.

HERNANDEZ, M.

ACTIVE

5 R01 CA 00000-08 (Hernandez)	4/1/2007 – 3/31/2017	3.6 academic
NIH/NCI	$110,532	3.0 summer
Gene Therapy for Small Cell Lung Carcinoma		

The major goals of this project are to use viral strategies to express the normal p53 gene in human SCLC cell lines and to study the effect on growth and invasiveness of the lines.

(NEW)
5 P01 CA 00000-02 (Chen) 7/1/2011 – 6/30/2016 1.8 academic
NIH/NCI $104,428 (sub only)
Mutations in p53 in Progression of Small Cell Lung Carcinoma

The major goals of this subproject are to define the p53 mutations in SCLC and their contribution to tumor progression and metastasis.

BE 00000 (Hernandez) 9/1/1999 – 8/31/2016 1.8 academic
American Cancer Society $86,732
p53 Mutations in Breast Cancer

The major goals of this project are to define the spectrum of p53 mutations in human breast cancer samples and correlate the results with clinical outcome.

(THIS AWARD)
2 R01 HL 000000-13 (Anderson) 3/1/2002 – 2/28/2017 0.6 calendar
NIH/NHLBI $186,529
Chloride and Sodium Transport in Airway Epithelial Cells

OVERLAP There was scientific overlap between aim 2 of 5 R01 CA 00000-08 and aim 4 of project 2 in 5 P01 CA 00000-02. In conjunction with agency staff, it was decided to remove aim 4 of project 2 from the P01 and adjust the budget and PI level of effort accordingly.

Special Instructions for Joint University and Department of Veterans Affairs (VA) Appointments

Individuals with joint university and VA appointments may request the university's share of their salary in proportion to the effort devoted to the research project. The individual's salary with the university determines the base for computing that request. Signature by the Institutional official on the application certifies that: (1) the individual is applying as part of a joint appointment specified by a formal Memorandum of Understanding between the university and the VA; and (2) there is no possibility of dual compensation for the same work, or of an actual or apparent conflict of interest regarding such work. Additional information may be requested by the awarding component(s).

1.9 Graduate Student Compensation

The maximum amount NIH will award for the support of a graduate student on a research grant or a cooperative agreement is tied to the National Research Service Award (NRSA) zero-level stipend in effect at the time the grant award is issued. The schedule for NRSA stipends can be found at http://grants.nih.gov/training/nrsa.htm. As required by 45 CFR 75.466, the compensation of graduate students supported by research grants must be reasonable. These operating principles associated with the compensation of students performing necessary work on NIH funded research projects are described in detail in the *NIH Grants Policy Statement* at http://grants.nih.gov/grants/policy. The amount provided for compensation includes salary or wages, fringe benefits, and tuition remission.

These guidelines apply to graduate students at the grantee institution who are supported by NIH research grants and cooperative agreements and not to individuals supported by NRSA training grants and fellowships. NIH has separate appropriations to support research training under the NRSA authorization at Section 487 of the Public Health Service Act.

The stipends provided to recipients of NRSA support offset the cost-of-living during the period of training and are not considered equivalent to salaries or other forms of compensation provided to individuals supported on research grants. Nevertheless, the entry-level postdoctoral NRSA stipend provides a useful benchmark for an award amount that approximates a reasonable rate of compensation for graduate students. Anticipated escalations in NRSA stipends (see http://grants.nih.gov/training/nas_report/NIHResponse.htm) in future years should permit annual increases in the maximum award amount for such individuals.

For all new and competing grant and cooperative agreement awards, the NIH will provide reasonable amounts for graduate compensation, consistent with the requested budget for the position(s) and up to the currently effective NRSA zero postdoctoral stipend level. NIH staff will review the compensation requested for graduate students on competing and cooperative agreement applications for which a detailed budget is submitted. NIH will neither request nor accept budgets for those applications using a modular budget format solely for the purpose of reviewing graduate student compensation. However, applicants should use this policy when estimating the number of modules.

When submitting detailed budgets that request support for a graduate student, grantees are reminded to request actual institutional-based compensation and to provide information justifying the requested compensation level. If this information is not provided, NIH staff will obtain this information from the institution's business office for any request that appears excessive.

NIH Institutes and Centers will review the requested compensation level and, if considered reasonable, will award the actual amount requested, up to a maximum equal to the NRSA zero level postdoctoral stipend. Revised budgets submitted solely to adjust requested levels for graduate students will not be accepted.

Institutions may continue to rebudget funds to charge more than the awarded amount provided that OMB cost principles requiring reasonable compensation are observed. In general, graduate student compensation will not be considered reasonable if in excess of the amount paid to a first-year postdoctoral scientist at the same institution performing comparable work.

1.10 DUNS Number & SAM Registration

All applicant organizations **must have** a Dun and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for Federal grants or cooperative agreements. For electronic SF424 (R&R) and paper-based PHS398 applications, see also instructions in Part I of the application guide. 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 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 PD/PIs do not need to register for a DUNS number.

Additionally, all NIH grantees must notify potential first-tier subrecipients that no entity may receive a first-tier subaward unless the entity has provided its DUNS number to the prime grantee organization.

All applicant and grantee organizations must maintain an active registration in the System for Award Management (SAM); formerly Central Contractor Registry Database (CCR).

Organizations that have not registered with SAM will need to obtain a DUNS number first and then access the SAM online registration through the SAM site at https://www.sam.gov/portal/public/SAM (U.S. organizations will also need to provide an Employer Identification Number from the Internal Revenue Service that may take an additional 2-5 weeks to become active). Because of the switch between CCR and SAM, registration can take several weeks to complete. Applicants are strongly encouraged to begin this registration process at least six weeks before any submission date.

For additional information regarding the use of DUNS numbers and maintaining an active SAM registration, please see NIH Guide Notice NOT-OD-11-004.

1.11 Public Access Policy

The Public Access Policy ensures that the public has access to the published results of NIH funded research at the NIH National Library of Medicine's (NLM) PubMed Central (PCM), a free digital archive of full-text biomedical and life sciences journal literature [http://www.pubmedcentral.nih.gov/]. Under the Policy NIH-funded investigators are required by Federal law to submit (or have submitted for them) to PMC an electronic version of the final, peer-reviewed manuscript upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. The author's final peer-reviewed manuscript is defined as the final version accepted for journal publication on or after 4/7/2008, and includes all modifications from the publishing peer review process, and all graphics and supplemental material associated with the article. Institutions and investigators are responsible for ensuring that any publishing or copyright agreements concerning submitted articles fully comply with this Policy. Applicants citing articles in NIH applications, proposals, and progress reports that fall under the Policy, were authored or co-authored by the applicant and arose from NIH support must include the PubMed Central reference number (PCMID) or NIH Manuscript Submission reference number (NIHMS ID).

This policy applies to all peer-reviewed articles resulting from research supported in whole or in part with direct costs from NIH, including research grant and career development awards, cooperative agreements, contracts, Institutional and Individual Ruth L. Kirschstein National Research Service Awards, SBIR/STTR awards, and NIH intramural research studies.

Additional information can be found at: http://publicaccess.nih.gov/.

1.12 PHS Metric Program

Consistent with Government-wide implementing regulations, 15 CFR part 19, Subpart B and/or any other Government-wide requirements, PHS policy is to support Federal transition to the metric system and to use the metric system of measurement in all grants, cooperative agreements, and all other financial assistance awards.

Likewise, measurement values in reports, publications, and other communications regarding grants will be in metric.

1.13 Transition to the SF424 (R&R) Application and Electronic Submission through Grants.gov

As first announced in August 2005 (NOT-OD-05-067), NIH is transitioning from the PHS 398 application to the SF424 (R&R) application and electronic submission through Grants.gov. This transition is being done by activity code. Applicants should refer to the Timeline to determine when a particular activity code has transitioned to the new form and electronic submission. Information on Transition Strategy and Timeline can be found at: http://grants.nih.gov/grants/ElectronicReceipt/files/timeline_NIH_transitions.pdf.

For more information on NIH's transition plans, see the Web site for Electronic Submission of Grant Applications: http://grants.nih.gov/grants/ElectronicReceipt/.

1.14 Multiple Program Director/Principal Investigator Policy

Multiple Program Director/Principal Investigator (multiple PD/PI) awards are an opportunity for multidisciplinary efforts and collaboration through a team of scientists under a single grant award. The applicant organization may designate multiple individuals as PD/PIs who share the authority and responsibility for leading and directing the project, intellectually and logistically. Each PD/PI is responsible and accountable to the applicant organization, or, as appropriate, to a collaborating organization, for the proper conduct of the project or program including the submission of all required reports. The presence of more than one identified PD/PI on an application or award diminishes neither the responsibility nor the accountability of any individual PD/PI. The applicant/grantee organization is responsible for securing and retaining the required written assurance signatures from each identified PD/PI on all applications, post-submission information, progress reports, and post-award prior approval requests and must make these signatures available to NIH or other authorized HHS or Federal officials upon request.

Applications designating multiple PD/PIs must include a Multiple PD/PI Leadership Plan describing the rationale for choosing the multiple PD/PI approach, and the governance and organizational structure of the leadership team. Do not submit a leadership plan if you are not submitting a Multiple PD/PI application.

Applications submitted electronically through Grants.gov for most award activity codes permit multiple PD/PIs, with the exception of awards for which multiple PD/PIs would not be appropriate such as individual fellowship and career awards, dissertations grants (R36), Pioneer Awards (DP1), Construction Grants (C06/UC6), Grants for Repair, Renovation and Modernization of Existing Research Facilities (G20), and Shared Instrumentation Grants (S10). See http://grants.nih.gov/grants/multi_pi/index.htm and NOT-OD-07-017 for additional information.

1.15 New, Including Early Stage, Investigators

NIH encourages all New Investigators to apply for R01 awards. The involvement of New Investigators is considered essential to the vitality of health-related research and has been addressed by several important NIH programs and studies which are detailed on the New Investigator Web site at http://grants.nih.gov/grants/new_investigators/index.htm. A New Investigator is one who has not previously competed successfully as a PD/PI for a significant NIH independent research award (see complete definition at http://grants.nih.gov/grants/new_investigators/index.htm#definition).

To encourage earlier application for NIH R01grant support, NIH identifies Early Stage Investigators (ESI). An ESI is a New Investigator who is within 10 years of completing his/her terminal research degree or is within 10 years of completing medical residency (or the equivalent). Applications from New Investigators and ESIs are identified and their career stage is considered at the time of review and award. The procedures for requesting as

extension of the ESI period and the conditions under which extensions will be considered are in NOT-OD-09-034.

See NOT-OD-08-121, NOT-OD-09-013, and NOT-OD-09-021 for additional information.

1.16 Policy on Instruction in the Responsible Conduct of Research

NIH requires that all trainees, fellows, participants, and scholars receiving support through any NIH training, career development award (individual or institutional), research education grant, and dissertation research grant must receive instruction in responsible conduct of research. These mechanisms include: D43, D71, F05, F30, F31, F32, F33, F34, F37, F38, K01, K02, K05, K07, K08, K12, K18, K22, K23, K24, K25, K26, K30, K99/R00, KL1, KL2, R25, R36, T15, T32, T34, T35, T36, T37, T90/R90, TL1, TU2, and U2R. This policy also applies to any other NIH-funded programs supporting research training, career development, or research education that require instruction in responsible conduct of research as stated in the relevant FOA.

A. Instructional Components

NIH recognizes that instruction in responsible conduct of research occurs formally and informally in educational settings and that informal instruction occurs throughout the research training experience. The guidance provided below is directed at formal instruction in responsible conduct of research and describes the accumulated experiences and the best practices of the scientific community over the past two decades.

1. **Format:** Substantial face-to-face discussions among the participating trainees/fellows/scholars/participants; a combination of didactic and small-group discussions (e.g. case studies); and participation of research training faculty members in instruction in responsible conduct of research are highly encouraged. While on-line courses can be a valuable supplement to instruction in responsible conduct of research, online instruction is not considered adequate as the sole means of instruction. A plan that employs only online coursework for instruction in responsible conduct of research will not be considered acceptable, except in special instances of short-term training programs (see below), or unusual and well-justified circumstances.
2. **Subject Matter:** While there are no specific curricular requirements for instruction in responsible conduct of research, the following topics have been incorporated into most acceptable plans for such instruction:
    a. conflict of interest – personal, professional, and financial
    b. policies regarding human subjects, research involving live vertebrate animals, and safe laboratory practices
    c. mentor/mentee responsibilities and relationships
    d. collaborative research including collaborations with industry
    e. peer review
    f. data acquisition and laboratory tools; management, sharing and ownership
    g. research misconduct and policies for handling misconduct
    h. responsible authorship and publication
    i. the scientist as a responsible member of society, contemporary ethical issues in biomedical research, and the environmental and societal impacts of scientific research

    While courses related to professional ethics, ethical issues in clinical research, or research involving vertebrate animals may form a part of instruction in responsible conduct of research, they generally are not sufficient to cover all of the above topics.

3. **Faculty Participation:** Training faculty and sponsors/mentors are highly encouraged to contribute both to formal and informal instruction in responsible conduct of research. Informal instruction occurs in the course of laboratory interactions and in other informal situations throughout the year. Training faculty may contribute to formal instruction in responsible conduct of research as discussion leaders, speakers, lecturers, and/or course directors. Rotation of training faculty as course directors, instructors, and/or discussion leaders may be a useful way to achieve the ideal of full faculty participation in formal responsible conduct of research courses over a period of time.
4. **Duration of Instruction:** Instruction should involve substantive contact hours between the trainees/fellows/scholars/participants and the participating faculty. Acceptable programs generally involve at least eight contact hours. A semester-long series of seminars/programs may be more effective than a single seminar or one-day workshop because it is expected that topics will then be considered in sufficient depth, learning will be better consolidated, and the subject matter will be synthesized within a broader conceptual framework.
5. **Frequency of Instruction:** Reflection on responsible conduct of research should recur throughout a scientist's career: at the undergraduate, post-baccalaureate, predoctoral, postdoctoral, and faculty levels. Institutional training programs and individual fellows/scholars are strongly encouraged to consider how to optimize instruction in responsible conduct of research for the particular career stage(s) of the individual(s) involved. Instruction must be undertaken at least once during each career stage, and at a frequency of no less than once every four years. It is highly encouraged that initial instruction during predoctoral training occurs as early as possible in graduate school. Individuals at the early career investigator level (including mentored K awardees and K12 scholars) must receive instruction in responsible conduct of research at least once during this career stage. Senior fellows and career award recipients (including F33, K02, K05, and K24 awardees) may fulfill the requirement for instruction in responsible conduct of research by participating as lecturers and discussion leaders. To meet the above requirements, instruction in responsible conduct of research may take place, in appropriate circumstances, in a year when the trainee, fellow or career award recipient is not actually supported by an NIH grant. This instruction can be documented as described below.

B. Special Considerations by Type of Award

Institutional training and institutional career development programs (for example, T15, T32, T34, T90/R90, TL1, K12, or K30 programs): Institutional programs are encouraged to provide instruction in responsible conduct of research for all individuals associated with the program of training regardless of their source of support.

Short-term training and research education programs (for example, T35 and R25 programs lasting six or fewer months, short-term trainees supported on T15, T32 and T34 programs, and short-term participants in R25 programs): The duration of RCR instruction within short-term institutional programs should be appropriate for the total duration of the program and should be justified in the application and is an instance where on-line instruction could be appropriate. Such programs may also use innovative strategies to incorporate instruction in responsible conduct of research and to relate instruction in responsible conduct of research to the scientific focus of the short-term program.

Individual awards: In keeping with the individual nature of these programs, fellows and scholars, along with their institutions and sponsors/mentors, are encouraged to tailor instruction in responsible conduct of research to the needs of the individual. Thus, instruction may go beyond formal institutional courses and provide opportunities for the individual to develop their own scholarly understanding of the ethical issues associated with their research activities and their impact on society. An individualized plan would be appropriate in the rare instances where an institution does not have an established formal mechanism for such instruction.

Applications lacking a plan for instruction in responsible conduct of research will be considered incomplete and may be delayed in the review process or not reviewed. Applications with unacceptable plans will not be funded until the applicant provides an acceptable, revised plan. For additional instructions, see the specific FOA. For funded grants, information on the nature of the instruction in the responsible conduct of research and the extent

of participating trainees/fellows/scholars/participants and faculty participation also must be provided in the annual progress report submitted as a prerequisite to receiving non-competing continuation support.

Additional information, including resources on Instruction in Responsible Conduct of Research, can be found in NOT-OD-10-019.

1.17 Transparency Act Reporting

The Federal Funding Accountability and Transparency Act of 2006 (FFATA), ensures that the public can access information on all entities and organizations receiving Federal funds. Central to the law was the development of www.USASpending.gov, a publicly available Web site with searchable information on each Federal grant and contract over $25,000. Moving one step further, reporting on executive compensation and first-tier subawards has been implemented as of October 1, 2010 with the development of the Federal Subaward Reporting System (FSRS). While NIH is responsible for providing award information to USASpending, grantees are responsible for entering their executive compensation and subaward information into FSRS.gov.

For additional information regarding subaward and executive compensation reporting requirements, please see NIH Guide Notice NOT-OD-11-005 and NIH Guide Notice NOT-OD-12-010.

1.18 Expectation for Institutions to Develop Individual Development Plans for Graduate Students and Postdoctoral Researchers

In an effort to assist graduate students and post-doctoral researchers achieve their career goals and become contributing members of the biomedical workforce, NIH encourages grantees to develop an institutional policy requiring that an Individual Development Plan (IDP) be implemented for every graduate student and postdoctoral research supported by any NIH grant and reportable on the progress report, regardless of the type of NIH grant that is used for support. While this is an expectation that should be broadly implemented by institutions for all graduate students and postdoctoral researchers supported by NIH, the actual reporting of the implementation of this expectation will be applicable primarily to those programs using the RPPR. As additional programs transition to the RPPR, this expectation will also apply to those submissions. Grantees are encouraged to report in RPPR *Section B. Accomplishments*, Question B.4 the use of the IDP for graduate students and/or postdoctoral researchers included in RPPR *Section D*. Participants or on a Statement of Appointment Form (PHS 2271). Do not include the actual IDP; instead include information to document that IDPs are used to help manage the training for those individuals. For Institutional Training Grants that use the PHS2590 progress report, information to document that IDPs are used to help manage the training for graduate student and postdoctoral trainees should be included under *Section 5.1.6 Progress Report Summary, Item A. Training Program.*

2. Assurances and Certifications

Each application to the PHS requires that the assurances and certifications in this section be verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application. For electronic SF424 (R&R) applications, this is verified by checking the “I agree” box on line 17 of the SF424 (R&R) Cover Form.

PD/PI (including Fellowship Applicant) and SO Verification

After the PD/PI and SO successfully submit an application electronically through Grants.gov, they will receive an automatically generated e-mail requesting them to view and verify (or reject) the application on-line in the Commons. To do this, the PI and SO need to:

1. Make sure they can log onto the eRA Commons. Before they receive the e-mail, they should be sure to know their Commons account names and passwords.
2. Verify the electronic grant application via the eRA Commons. Complete instructions on the verification process are in the Applicant Package.

All assurances listed below may or may not be applicable to the project, program, or type of applicant organization. Applicants and grantees must comply with a number of additional public policy requirements. Refer to the *NIH Grants Policy Statement* (http://grants.nih.gov/grants/policy/policy.htm) for additional information.

2.1 Human Subjects Research

See Part II, 5. Human Subjects Research Policy

2.2 Vertebrate Animals

The *PHS Policy on Humane Care and Use of Laboratory Animals* (PHS Policy) mandates that an approved Animal Welfare Assurance must be on file with OLAW at the time of award for all grantee organizations receiving PHS support to conduct research involving live vertebrate animals. The PHS Policy requires grantee organizations to establish appropriate policies and procedures to ensure the humane care and use of animals. The PHS Policy stipulates that the grantee organization, whether domestic or foreign, bears responsibility for the humane care and use of animals in PHS supported research activities. This policy incorporates the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training* and requires that institutions base their animal care and use programs on the *Guide for the Care and Use of Laboratory Animals*. This policy does not supersede state or local laws or regulations that impose more stringent standards for the care and use of laboratory animals. All institutions are required to comply with the applicable regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act, and other federal statutes and regulations relating to animals. (See these documents at http://grants.nih.gov/grants/olaw/olaw.htm).

The PHS Policy defines *animal* as any live vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes. The generation of custom antibodies constitutes an activity involving vertebrate animals.

In addition to an OLAW-approved Animal Welfare Assurance, the grantee organization must provide verification that the IACUC has reviewed and approved the proposed activity. IACUC approval must have been granted within three years to be valid. IACUCs are not authorized to administratively extend approval beyond three years. Verification of IACUC approval is requested under Just-in-Time policy (prior to award) (see 1.7). Foreign grantees receiving direct support are not required to provide IACUC approval, but must have an approved Animal Welfare Assurance for Foreign Institutions (Foreign Assurance). See a sample Foreign Assurance at: http://grants.nih.gov/grants/olaw/sampledoc/foreign.htm.

Under consortium (subaward) agreements in which the grantee collaborates with one or more other organizations, the grantee, as the direct and primary recipient of NIH grant funds, is accountable for the performance of the project, the appropriate expenditure of grant funds by all parties, and all other obligations of the grantee as specified in the NIHGPS (See NIH GPS, Part II, Terms and Conditions of NIH Grant Awards, Consortium Agreements). The animal welfare requirements that apply to grantees also apply to consortium participants and subprojects. The prime grantee is responsible for including these requirements in its agreements with collaborating organizations, and for ensuring that all sites engaged in research involving the use of live vertebrate animals have an approved Animal Welfare Assurance and that the activity has a valid IACUC approval. See a sample Domestic Assurance at: http://grants.nih.gov/grants/olaw/sampledoc/assur.htm

If the prime grantee does not have an animal care and use program, facilities to house animals and conduct research on site, or an IACUC and the animal work will be conducted at a Project/Performance Site with an

Animal Welfare Assurance, the grantee must obtain an Inter-institutional Assurance from OLAW. See a sample Interinstitutional Assurance at: http://grants.nih.gov/grants/olaw/sampledoc/interinstitutional_assurance.htm

When the grantee is a domestic institution and there is a foreign Project/Performance Site using animals, the grantee must ensure that the Project/Performance Site has an approved Animal Welfare Assurance and must provide verification of IACUC approval by the domestic grantee's IACUC. This is to certify to NIH that the activity as conducted at the foreign Project/Performance Site is acceptable to the grantee organization. Foreign applicant organizations applying for PHS awards for activities involving vertebrate animals must comply with the *International Guiding Principles for Biomedical Research Involving Laboratory Animals* (http://grants.gov/grants/olaw/Guiding_Principles_2012.pdf) and all laws, regulations and policies governing the care and use of laboratory animals in the jurisdiction in which the research will be conducted.

For additional details regarding completion of the Vertebrate Animals Section of the Research Plan, see http://grants.nih.gov/grants/olaw/VAChecklist.pdf.

2.2.1 Research Involving Chimpanzees

NIH established a panel, which is independent of the existing NIH review processes (e.g., peer review of grants), to consider whether requests to the NIH to use chimpanzees in research are consistent with principles and criteria established by the Institute of Medicine (IOM). A working group of the NIH Council of Councils, the Chimpanzee Research Use Panel (CRUP or "Panel") was created and is charged with considering requests to use chimpanzees in research. The CRUP convenes before the NIH makes decisions about funding or otherwise allowing research involving chimpanzees but after the NIH peer review is completed for grant applications. Certain observational or non-interventional research involving chimpanzees and certain research involving chimpanzee biomaterials is exempt from the CRUP's consideration.

The Chimpanzee Research Use Form is used by the NIH to obtain additional information from the applicant about the proposed use of chimpanzees for research. The NIH contacts applicants to complete the Chimpanzee Research Use Form when the proposed research involves the use of chimpanzees and/or chimpanzee biomaterials and the application is being considered for funding by an NIH IC. Completion of this form is a mandatory step for research involving chimpanzees. Failure to complete this form will prevent the agency from taking funding action on a research project involving chimpanzees or otherwise allowing the research to proceed. Information about the CRUP is available at http://dpcpsi.nih.gov/council/crup. Details about the form are available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-024.html.

Note: Research applications proposing the use of chimpanzees in research could experience extra time needed to complete the pre-award process. Investigators planning to conduct chimpanzee research should submit the grant application at least 12 months before funding is needed.

2.3 Debarment and Suspension

HHS regulations published in 2 CFR 376 implement the government-wide debarment and suspension system guidance (2 CFR 180) for HHS' non-procurement programs and activities. "Non-procurement transactions" include, among other things, grants, cooperative agreements, scholarships, fellowships, and loans. NIH implements the HHS Debarment and Suspension regulations as a term and condition of award. Accordingly, recipients of NIH grants ("primary covered transactions"), including sponsoring institutions for Kirschstein-NRSA individual fellowships, are required to determine whether it or any of its principals (as defined in 2 CFR 180.995 and 2 CFR 376.995) are excluded or disqualified from participating in a covered transaction (i.e., grant or cooperative agreement) prior to entering into the covered transaction, i.e., prior to the drawdown of funds which signals acceptance of the grant award. Grantees may decide the method and frequency by which this determination is made and may check excluded parties in SAM, although checking SAM is not required.

Prior to the drawdown of funds for each grant award, grantees must report to the funding IC if the grantee or any of its principals:

- Are presently excluded or disqualified;

- Have been convicted within the preceding three years of any of the offenses listed in 2 CFR 180.800(a) or had a civil judgment for one of those offenses within that time period;
- Are presently indicted for or otherwise criminally or civilly charged by a governmental entity (Federal, State, or local) with commission of any of the offenses listed in 2 CFR 180.800(a); or
- Have had one or more public transactions (Federal, State, or local) terminated within the preceding three years for cause or default.

Disclosure of unfavorable information by grantees under this requirement will not necessarily cause NIH to deny participation in the grant. NIH will consider the information when determining whether to enter into the covered transaction. NIH will also consider any additional information or explanation that grantees elect to submit with the disclosed information. However, if it is later determined that a grantee failed to disclose information that it knew at the time it accepted the NIH grant award, NIH may (a) terminate the transaction for material failure to comply with the terms and conditions of the award or (b) pursue any other available remedies, including suspension and debarment.

Grantees must immediately report to the NIH funding IC if at any time during the project period, including periods of no-cost extension, they discover that they (a) failed to disclose information prior to the drawdown of funds or (b) due to changed circumstances the grantee or any of its principals for the grant now meet the reporting criteria.

"Lower tier" transactions (e.g., consortiums, subcontracts, consultants, collaborators, and contractors that require the provision of goods or services that will equal or exceed $25,000) also are subject to the HHS regulations. Prior to entering into a lower tier covered transaction with a participant (as defined in 2 CFR 180.980), grantees must verify that the person (as defined in 2 CFR 180.985) is not excluded or disqualified. Grantees may not enter into any transaction with a person who is disqualified from that transaction unless an exception under the disqualifying statue, Executive Order, or regulation has been obtained from HHS.

Grantees must require participants at the next lower tier to (a) comply with the HHS Debarment and Suspension regulations as a condition of participation in the transaction and (b) pass the requirement to comply with the HHS Debarment and Suspension regulations to each person involved in the covered transaction at the next lower tier. Likewise, before entering into such a transaction lower tier participants and contractors under grants (where the contract requires the provision of goods or services that will equal or exceed $25,000) must report to the grantee if it or any participants are presently excluded or disqualified.

Grantees also are required to assure compliance for each trainee under a Kirschstein-NRSA institutional research training grant, or other similar NIH-supported institutional training grant, before their appointment.

Organizations or individuals that are suspended, debarred, or voluntarily excluded from eligibility cannot receive NIH grants, be paid from NIH grant funds, whether under a primary or lower-tier transaction (including trainees on NIH-supported training grants), or otherwise participate during the period of suspension, debarment, or exclusion. Because individuals who have been debarred, suspended, declared ineligible, or voluntarily excluded from covered transactions may not receive Federal funds for a specified period of time, charges made to the NIH grants for such individuals (e.g., salary) are unallowable.

2.4 Drug-Free Workplace

The Drug-Free Workplace Act of 1988 (41 U.S.C. § 701 et seq.) requires that all organizations receiving grants from any Federal agency agree to maintain a drug-free workplace. By signing the application, the AOR agrees that the grantee will provide a drug-free workplace and will comply with the requirement to notify NIH if an employee is convicted of violating a criminal drug statute. Failure to comply with these requirements may be cause for debarment. Government wide requirements for Drug-Free Workplace for Financial Assistance are found in 2 CFR 182; HHS implementing regulations are set forth in 2 CFR 382.400. All recipients of NIH grant funds must comply with the requirements in Subpart B (or Subpart C if the recipient is an individual) of part 382.

2.5 Lobbying

a) Recipients of Federal grants, cooperative agreements, contracts, and loans are prohibited by 31 U.S.C. 1352, "Limitation on use of appropriated funds to influence certain Federal contracting and financial transactions," from using appropriated Federal funds to pay any person for influencing or attempting to influence any officer or employee of an agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress with respect to the award, continuation, renewal, amendment, or modification of any of these instruments. These requirements are implemented for HHS in 45 CFR 93, which also describes types of activities, such as legislative liaison activities and professional and technical services, which are not subject to this prohibition under certain circumstances.

Applicants for NIH awards are required to certify and disclose that they:

- have not made, and will not make, such a prohibited payment;
- used or will use non-appropriated funds if they have made or agreed to make such payment; and
- will include these requirements in consortium agreements and contracts under grants that will exceed $100,000 and obtain necessary certifications from those consortium participants and contractors.

Certifications and disclosures must be filed at the times prescribed in the regulations based on the expected total costs.

The signature of the AOR on the application serves as the required certification of compliance for the applicant organization.

Standard Form LLL, "Disclosure of Lobbying Activities," its instructions, and continuation sheet is available at http://www.whitehouse.gov/sites/default/files/omb/assets/omb/grants/sflllin.pdf.

b) Appropriation Prohibition: In addition to the HHS implementation described in section a) above, grants are also subject to the Lobbying Prohibition found in the annual HHS appropriations. This requirement was expanded in 2012 and now indicates that NIH appropriated funds may not be used, other than for normal and recognized executive-legislative relationships for publicity or propaganda purposes, for the preparation, distribution, or use of an kit, pamphlet, booklet, publication, electronic communication, radio, television, or video presentation designed to support or defeat the enactment of legislation before the Congress or any State or local legislature or legislative body, except in presentation to the Congress or any State legislature or local legislature itself or designed to support or defeat any proposed or pending regulation administrative action, or order issued by the executive branch of any State or local government, except in presentation to the executive branch of any State or local government itself. No part of any governing appropriation act shall be used to pay the salary or expenses of any grant or contract recipient, or agent acting for such recipient, related to any activity designed to influence the enactment of legislation, appropriations, regulation, administrative action, or Executive Order proposed or pending before the Congress or any State government, State legislature or local legislature or legislative body other than for normal and recognized executive-legislative relationships or participation by an agency or officer of a State, local or tribal government in policymaking and administrative processes within the executive branch of that government. No part of any governing appropriation act shall be used for any activity to advocate or promote any proposed, pending or future Federal, State or local tax increase, or any proposed, pending, or future requirement or restriction on any legal consumer product, including its sale or marketing, including but not limited to the advocacy or promotion of gun control.

More information on this mandate can be found at http://grants.nih.gov/grants/lobbying_guidance.htm. Note this legislative mandate is subject to change on an annual basis. NIH annually posts information on legislative mandates at: http://grants1.nih.gov/grants/policy/appropriations_info.htm.

2.6 Non-Delinquency on Federal Debt

The Federal Debt Collection Procedure Act, 28 U.S.C. 3201 (e), provides that an organization or individual that is indebted to the United States, and has a judgment lien filed against it, is ineligible to receive a Federal grant. NIH cannot award a grant unless the Authorized Organization Representative of the applicant organization (or individual as in the case of an individual Ruth L. Kirschstein National Research Service Award) certifies, by means of his/her signature on the application, that the organization is not delinquent in repaying any Federal debt. If the applicant discloses delinquency on a debt owed to the Federal Government, NIH may not award the grant until the debt is satisfied or satisfactory arrangements are made with the agency to which the debt is owed.

2.7 Research Misconduct

Each institution that receives or applies for a research, research training, or research-related grant or cooperative agreement under the Public Health Service Act must certify that the institution has established administrative policies as required by 42 CFR part 93, "Public Health Service Policies on Research Misconduct."

The signature of the official signing for the applicant organization on the Face Page of the application (or for electronic applications, checking the "I agree box on line 17 of the SF424 (R&R) Cover Form) serves as certification that:

1. The institution will comply with the requirements of the PHS regulations for dealing with reporting possible research misconduct under 42 CFR part 93;
2. The institution has established policies and procedures incorporating the provisions set forth in 42 CFR part 93;
3. The institution will provide its policies and procedures to the Office of Research Integrity upon request; and
4. The institution will submit an Annual Report on Possible Research Misconduct (Form 6349). A copy of Form 6349, covering the previous year, will be automatically sent to all PHS awardees by the Office of Research Integrity each January.

Research Misconduct is defined by the Public Health Service as "fabrication, falsification or plagiarism in proposing, performing, or reviewing research, or in reporting research results."

(a) Fabrication is making up data or results and recording or reporting them.

(b) Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

(c) Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

(d) Research misconduct does not include honest error or differences of opinion.

For further information, please contact:

U.S. Dept. of Health and Human Services
Office of Research Integrity
1101 Wootton Parkway, Suite 750
Rockville, MD 20852
AskORI@osophs.hhs.gov
Phone: (240) 453-8200
Fax: (301) 443-5351

2.8 Assurance of Compliance (Civil Rights, Handicapped Individuals, Sex Discrimination, Age Discrimination)

Before a grant award can be made, a domestic applicant organization must certify that it has filed with the HHS Office for Civil Rights: an Assurance of Compliance (Form HHS 690) with Title VI of the Civil Rights Act of 1964 (P.L. 88352, as amended), which prohibits discrimination on the basis of race, color, or national origin; Section 504 of the Rehabilitation Act of 1973 (P.L. 93-112, as amended), which prohibits discrimination on the basis of handicaps; Title IX of the Education Amendments of 1972 (P.L. 92-318, as amended), which prohibits discrimination on the basis of sex; and the Age Discrimination Act of 1975 (P.L. 94-135), which prohibits discrimination on the basis of age.

The Assurance of Compliance Form HHS 690 is available from http://www.hhs.gov/ocr/civilrights/clearance/hhs690.pdf.

Assurance of Compliance Form HHS 690 is now used in lieu of individual assurances: Form HHS 441, Civil Rights; Form HHS 641, Handicapped Individuals; Form HHS 639-A, Sex Discrimination; and Form HHS 680, Age Discrimination.

2.8.1 Limited English Proficiency

EO 13166, August 11, 2000, requires grantees receiving Federal financial assistance to take steps to ensure that people with limited English proficiency can meaningfully access health and social services. A program of language assistance should provide for effective communication between the service provider and the person with limited English proficiency to facilitate participation in, and meaningful access to, services. The obligations of grantees are explained on the OCR Web site at http://www.hhs.gov/ocr/civilrights/resources/specialtopics/lep/.

2.9 Research Involving Recombinant or Synthetic Nucleic Acid Molecules, including Human Gene Transfer Research

The National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (*NIH Guidelines*) (March 2013 or latest revision) apply to all research projects (NIH-funded and non-NIH-funded) that involve recombinant or synthetic nucleic acid molecules and are conducted at or sponsored by an organization that receives NIH support for recombinant or synthetic nucleic acid research. A copy of the *NIH Guidelines* is available at http://oba.od.nih.gov/rdna/nih_guidelines_oba.html.

According to the *NIH Guidelines*, recombinant and synthetic nucleic acid molecules are defined as (1) molecule that: a) are constructed by joining nucleic acid molecules and b) can replicate in a living cell, i.e., recombinant nucleic acids, or (2) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids, or (3) molecules that result from the replication of those described in (1) or (2). The *NIH Guidelines* apply to both basic and clinical research studies. Specific guidance for the conduct of human gene transfer studies appears in Appendix M of the *NIH Guidelines*.

Failure to comply with these requirements may result in suspension or termination of an award for recombinant or synthetic nucleic acid molecule research at the organization, or a requirement for NIH prior approval of any or all recombinant or synthetic nucleic acid molecule projects at the organization. Two specific requirements of the *NIH Guidelines* are discussed below, but the grantee should carefully review the *NIH Guidelines* in their entirety to ensure compliance with all of the requirements for projects involving recombinant or synthetic nucleic acid molecules.

Recombinant or synthetic nucleic acid research involving select agents also is subject to pertinent CDC and USDA regulations, 42 CFR 73, Select Agents and Toxins; and 7 CFR 331 and 9 CFR 121, Possession, Use, and Transfer of Biological Agents and Toxins.

2.10 Financial Conflict of Interest

NIH requires grantees and investigators (except Phase I SBIR/STTR applicants and grantees) to comply with the requirements of 42 CFR part 50, Subpart F, "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought." A Final Rule amending this PHS regulation (and the companion regulation at 45 CFR part 94, "Responsible Prospective Contractors," imposing similar requirements for research contracts) was published on August 25, 2011 in the Federal Register (http://www.gpo.gov/fdsys/pkg/FR-2011-08-25/pdf/2011-21633.pdf). An Institution applying for or receiving PHS funding from a grant or cooperative agreement that is covered by the rule must be in full compliance with all of the revised regulatory requirements, and immediately upon making its institutional Financial Conflict of Interest (FCOI) policy publicly accessible as described in the regulation.

In checking the "I agree" box on line 17 of the SF424 (R&R) Form, the Authorized Organization Representative of the applicant organization certifies compliance with the requirements of 42 CFR part 50, Subpart F, including that:

1. There is in effect at the Institution an up-to-date, written and enforced administrative process to identify and manage FCOI with respect to all research projects for which NIH funding is sought or received;
2. The Institution shall promote and enforce Investigator compliance with the regulation's requirements including those pertaining to disclosure of Significant Financial Interests;
3. The Institution shall identify and manage FCOIs and provide initial and ongoing FCOI reports to the NIH consistent with this subpart;
4. When requested, the Institution will promptly make information available to the NIH/HHS relating to any Investigator disclosure of financial interests and the Institution's review of, and response to, such disclosure, whether or not the disclosure resulted in the Institution's determination of a FCOI;
5. The Institution shall fully comply with the requirements of the regulation.

When the Institution determines that an FCOI exists (as described above), the Institution must report to the NIH awarding IC through the submission of an initial and annual FCOI report using the eRA Commons FCOI Module. The initial FCOI report will include the following information:

- Grant number and PD/PI or Contact PD/PI if the grant is awarded under the multiple PI model;
- Name of Investigator (if different from the PD/PI) with the FCOI;
- Name of the entity with which the Investigator has an FCOI;
- Nature of the FCOI (e.g., consulting fees, honoraria, paid authorship, equity interest, intellectual property rights and interests, and reimbursed or sponsored travel);
- Value of the financial interest $0-4,999; $5,000-9,999; $10,000-19,999; amounts between $20,000-100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000 or a statement that a value cannot be readily determined;
- A description how the financial interest relates to the NIH-funded research and the basis for the Institution's determination that the financial interest conflicts with such research; and
- Key elements of the Institution's management plan, including:
    1. Role and principal duties of the conflicted Investigator in the research project;
    2. Conditions of the management plan;
    3. How the management plan is designed to safeguard objectivity in the research project;
    4. Confirmation of the Investigator's agreement to the management plan;
    5. How the management plan will be monitored to ensure Investigator compliance; and

6. Other information as needed.

The annual FCOI report must be submitted to NIH through the eRA Commons FCOI Module each year within a competitive segment or until the Institution reports the FCOI no longer exists. The annual FCOI report will include the following information:

- Status of the FCOI
- Changes to the management plan, if applicable

The information above is only a sample of the regulatory requirements found in 42 CFR part 50, Subpart F. Applicants must read the regulation in its entirety to ensure compliance with all of the requirements.

2.11 Smoke-Free Workplace

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and to promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

2.12 Prohibited Research

NIH Appropriation Acts have limited the use of NIH funding for a number of years and typically continue the same limitations from year to year. These legislative mandates appear in the Public Law 112-74 that authorizes NIH appropriations:

BAN ON FUNDING OF HUMAN EMBRYO RESEARCH (Section 508)

NIH is prohibited from using appropriated funds to support human embryo research. Grant, cooperative agreement, and contract funds may not be used for: "(a)…(1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR part 46.208(a)(2) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). (b) For purposes of this section, the term `human embryo or embryos' includes any organism not protected as a human subject under 45 CFR part 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells."

The NIH has published final guidelines on the allowability of Federal funds to be used for research on human embryonic stem cell lines at http://stemcells.nih.gov/Pages/Default.aspx.

LIMITATION ON USE OF FUNDS FOR PROMOTION OF LEGALIZATION OF CONTROLLED SUBSTANCES (Section 509)

"(a) None of the funds made available in this Act may be used for any activity that promotes the legalization of any drug or other substance included in schedule I of the schedules of controlled substances established by section 202 of the Controlled Substances Act (21 U.S.C.812). (b)The limitation in subsection (a) shall not apply when there is significant medical evidence of a therapeutic advantage to the use of such drug or other substance or that federally sponsored clinical trials are being conducted to determine therapeutic advantage."

RESTRICTION ON DISTRIBUTION OF STERILE NEEDLES (Section 523)

"Notwithstanding any other provision of this Act, no funds appropriated in this Act shall be used to carry out any program of distributing sterile needles or syringes for the hypodermic injection of any illegal drug."

RESTRICTION ON ABORTIONS (Section 506)

(a) None of the funds appropriated under this Act, and none of the funds in any trust fund to which funds are appropriated under this Act, shall be expended for any abortion."

(b) None of the funds appropriated in this Act, and none of the funds in any trust fund to which funds are appropriated in this Act, shall be expended for health benefits coverage that includes coverage of abortion.

(c) The term "health benefits coverage" means the package of services covered by a managed care provider or organization pursuant to a contract or other arrangement."

EXCEPTION TO RESTRICTION ON ABORTIONS (Section 507)

(a) The limitations established in the preceding section shall not apply to an abortion—

  (1) if the pregnancy is the result of an act of rape or incest; or

  (2) in the case where a woman suffers from a physical disorder, physical injury, or physical illness, including a life endangering physical condition caused by or arising from the pregnancy itself, that would, as certified by a physician, place the woman in danger of death unless an abortion is performed.

(b) Nothing in the preceding section shall be construed as prohibiting the expenditure by a State, locality, entity, or private person of State, local, or private funds (other than a State's or locality's contribution of Medicaid matching funds).

(c) Nothing in the preceding section shall be construed as restricting the ability of any managed care provider from offering abortion coverage or the ability of a State or locality to contract separately with such a provider for such coverage with State funds (other than a State's or locality's contribution of Medicaid matching funds).

(d)

  (1) None of the funds made available in this Act may be made available to a Federal agency or program, or to a State or local government, if such agency, program, or government subjects any institutional or individual health care entity to discrimination on the basis that the health care entity does not provide, pay for, provide coverage of, or refer for abortions.

  (2) In this subsection, the term ''health care entity'' includes an individual physician or other health care professional, a hospital, a provider-sponsored organization, a health maintenance organization, a health insurance plan, or any other kind of health care facility, organization, or plan.

2.13 Select Agent Research

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (42 U.S.C. 201) is designed to provide protection against misuse of select agents and toxins whether inadvertent or the result of terrorist acts against the United States homeland or other criminal acts. The Act was implemented, in part, through regulations published by HHS and USDA at 42 CFR 73, 9 CFR 121 and 7 CFR 331 or commonly referred to as "Select Agent Regulations." Copies of these regulations are available at http://www.selectagents.gov/Regulations.html, or can be obtained from CDC, 1600 Clifton Road, MS A-46, Atlanta, GA 30333; telephone: 404-718-2000.

Domestic grantees who conduct research involving select agents or toxins (see Section 3 and 4 of 42 CFR 73 and 9 CFR 121 and Section 3 of 7 CFR 331) must maintain a registration with CDC (or USDA, depending on the agent) before using NIH funds. No funds can be used for research involving select agents or toxins if the registration certificate maintained by CDC or USDA is suspended or revoked.

Foreign Institutions and International Organizations who conduct research involving select agents (see 42 CFR 73 for the select agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens) must provide information satisfactory to the NIH that a process equivalent to that described in 42 CFR 73 for U.S. institutions is in place and will be administered on behalf of all select agent work sponsored by NIH funds

before using these funds for any work directly involving select agents. Grantees must be willing to address the following key elements appropriate for their institutions: safety, security, training, procedures for ensuring that only approved/appropriate individuals have access to the select agents, and any applicable laws, regulations and policies equivalent to 42 CFR 73. If this work will not, in fact, involve select agents (e.g. excluded strains), and you provide documentation satisfactory to the NIH that your work does not now nor will it in the future (i.e. throughout the life of the award) involve select agents, no further action will be necessary.

Grantees who conduct research involving select agents (see 42 CFR 73 for the select agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens) must complete registration with CDC (or USDA, depending on the agent) before using NIH funds for any work directly involving the select agent at the U.S. institution. No funds can be used for research involving select agents if the final registration certificate is denied. Before using NIH funds for any work directly involving the select agents at a foreign subrecipient, the U.S. grantee must provide information from the foreign institution satisfactory to the NIH that a process equivalent to that described in 42 CFR 73 for U.S. institutions is in place and will be administered on behalf of all select agent work sponsored by these funds. Grantees must be willing to address the following key elements appropriate for the foreign institution: safety, security, training, procedures for ensuring that only approved/appropriate individuals have access to the select agents, and any applicable laws, regulations and policies equivalent to 42 CFR 73. If this work will not, in fact, involve select agents (e.g. excluded strains), and you provide documentation satisfactory to the NIH that your work does not now nor will it in the future (i.e. throughout the life of the award) involve select agents, no further action will be necessary.

In addition to the above requirements, research involving **both select agents and recombinant or synthetic nucleic acid molecules** is also subject to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*) (see Section 2.9 Research Involving Recombinant or Synthetic Nucleic Acid Molecules, including Human Gene Transfer Research in this subsection for applicability of these guidelines).

For additional information regarding select agent research, see the following Web sites maintained by NIH, CDC, and USDA:

NIH Office of Extramural Research Select Agent Information: http://grants.nih.gov/grants/policy/select_agent/

Federal Select Agent Program (CDC and USDA)
http://www.selectagents.gov/index.html

Federal Select Agent Program Resources: http://www.selectagents.gov/resources.html

Federal Select Agent Program Public Laws and Regulations: http://www.selectagents.gov/regulations.html

Federal Select Agent Program Related Links: http://www.selectagents.gov/links.html

Animal and Plant Health Inspection Service (APHIS) Select Agent Program:
https://www.aphis.usda.gov/wps/portal/aphis/ourfocus/planthealth?urile=wcm%3apath%3a%2Faphis_content_library%2Fsa_our_focus%2Fsa_animal_health%2Fsa_import_into_us%2Fsa_ag_select_agent%2Fct_agricultural_select_agent_program

2.13.1 Dual Use Research of Concern

On September 24, 2014, the Federal government issued a policy for the oversight of life sciences "Dual Use Research of Concern" (DURC). This policy will be implemented on all NIH competing and non-competing awards issued on or after September 24, 2015. In signing the application Face Page (or for electronic applications, by checking the “I agree” box on line 17 of the SF424 (R&R) Form), the Authorized Organization Representative (AOR) of the applicant organization certifies that the institution will comply with this policy. Applicant organizations also certify they will comply with this policy when submitting a Research Performance Progress Report (RPPR) for a non-competing continuation award.

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 policy applies to research that involves one or more of 15 agents listed in the policy that can also be reasonably anticipated to produce one or more of 7 effects described in the policy. Research involving these agents and effects will be reviewed by NIH to determine whether it meets the definition of DURC. For research that may be considered DURC, NIH will work collaboratively with the institution and investigators to develop a risk mitigation plan, which may be implemented through a term of award. For example, NIH may request that institutions periodically review a project for its DURC potential, propose any modifications to the risk mitigation plan, and share any resulting manuscripts with the designated awarding component's Program Official prior to submitting the manuscript to a journal.

For additional information regarding DURC:

- NIH Guide Notice NOT-OD-15-017: NIH Implementation of the US Government Policy on Institutional Oversight of Life Sciences Dual Use Research of Concern
- Public Health Emergency S3: Science, Safety, and Security program: http://www.phe.gov/s3/Pages/default.aspx
- NIH Biosecurity DURC website http://osp.od.nih.gov/office-biotechnology-activities/biosecurity/dual-use-research-concern

2.14 Program Director/Principal Investigator, Fellow and Sponsor Assurance

It is a compliance requirement that the applicant organization must secure and retain a written assurance from the PD/PI prior to submitting an application to the PHS. Therefore, organizations must retain a unique signature and date for each submitted application. This assurance must be available to the sponsoring agency or other authorized HHS or Federal officials upon request. Such an assurance must include at least the following certifications: 1) that the information submitted within the application is true, complete and accurate to the best of the PD/PI's knowledge; 2) that any false, fictitious, or fraudulent statements or claims may subject the PD/PI to criminal, civil, or administrative penalties; and 3) that the PD/PI agrees to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of the application. If multiple PD/PIs are proposed in an application, this assurance must be retained for all named PD/PIs.

Additionally, for the Fellow and Sponsor on individual Fellowship applications, it is a compliance requirement that the applicant organization must secure and retain a written assurance from the Fellow and Sponsor prior to submitting an application to the PHS. Therefore, organizations must retain a unique signature and date for each submitted application. This assurance must be available to the sponsoring agency or other authorized HHS or Federal officials upon request. Such an assurance must include at least the following certifications: (1) that the information submitted within the application is true, complete and accurate to the best of the Fellow's and Sponsor's knowledge; (2) that any false, fictitious, or fraudulent statements or claims may subject the Fellow and Sponsor to criminal, civil, or administrative penalties; (3) that the Sponsor will provide appropriate training, adequate facilities, and supervision if a grant is awarded as a result of the application; (4) that the Fellow has read the Ruth L. Kirschstein National Research Service Award Payback Assurance (See link below, section I. Service Requirement) and will abide by the Assurance if an award is made; and (5) that the award will not support residency training.

Other helpful links:
Guide Notice for Payback Obligation: http://grants.nih.gov/grants/guide/notice-files/not93-201.html
Full Payback Agreement: http://grants.nih.gov/grants/funding/416/phs6031.doc.

2.15 Impact of Grant Activities on the Environment and Historic Properties

All NIH grants, whether or not they include construction or major alteration and renovation activities, are subject to the requirements of the National Environmental Policy Act of 1969 (NEPA), as amended. This Act requires Federal agencies to consider the probable environmental consequences of all grant-supported activities. As part of NIH's implementation of this Act, grantees are required to promptly notify NIH of any probable impacts on the environment from grant-supported activities, or certify that no such activities exist upon receipt of a grant award. In addition, NIH has determined that most NIH research grants are not expected to individually or cumulatively have a significant effect on the environment unless any part of the proposed research and/or project includes one or more of the following categorical exclusions listed below:

1. The potential environmental impacts of the proposed research may be of greater scope or size than other actions included within a category.
2. The proposed research threatens to violate a Federal, State, or local law established for the protection of the environment or for public health and safety.
3. Potential effects of the proposed research are unique or highly uncertain.
4. Use of especially hazardous substances or processes is proposed for which adequate and accepted controls and safeguards are unknown or not available.
5. The proposed research may overload existing waste treatment plants due to new loads (volume, chemicals, toxicity, additional hazardous wasted, etc.).
6. The proposed research may have a possible impact on endangered or threatened species.
7. The proposed research may introduce new sources of hazardous/toxic wastes or require storage of wastes pending new technology for safe disposal.
8. The proposed research may introduce new sources of radiation or radioactive materials.
9. Substantial and reasonable controversy exists about the environmental effects of the proposed research.

This requirement is in addition to the other public policy requirements for grants for construction and alteration and renovation activities discussed more fully in the NIH Grants Policy Statement, Subpart B, 10. Construction, Modernization, or Major Alteration and Renovation of Research Facilities.

Additionally, all NIH grant awards should not involve activities that violate provisions of the National Historic Preservation Act of 1966 or other statutory requirements. All grantees are subject to the requirements of Executive Order 13287 – Preserve America, requiring notification to NIH of all activities that would affect any historic property, or certification that no impact will occur upon receipt of the grant award or in a post-award action without NIH prior approval. For the purposes of the Order, historic property is defined to include any prehistoric or historic district, site, or object included in, or eligible for inclusion in, the National Register of Historic Places maintained by the Secretary of the Interior. This term includes artifacts, records, and remains that are related to and located within such properties. The term includes properties of traditional religious and cultural importance to an Indian tribe or Native Hawaiian organization and that meet the National Register criteria.

2.16 Institutions Receiving Awards for Training of Graduate Students for Doctoral Degrees

As required by Section 403C of the Public Health Service Act, each institution receiving an NIH award for the training of graduate students for doctoral degrees must provide information on completion rates and time to degree to all applicants to doctoral programs supported by NIH training awards. Specifically, institutions must provide applicants with the following information for the programs to which they apply:

- The percentage of students admitted for study who successfully attain a doctoral degree, and
- The average time (not including any leaves of absence) between the beginning of graduate study and the receipt of a doctoral degree.

Institutions **affected** by this Assurance and information disclosure requirement are doctoral degree granting institutions that receive any of the following institutional training grant awards or cooperative agreements from the NIH for the doctoral training of graduate students:

D43, TU2, T15, T32, T37, T90, U2R, U90, and U54/TL1

Institutions are **not affected** by this requirement if they:

- Receive only individual NIH fellowship awards.
- Provide training only to undergraduate or master's level students supported through one of the activity codes listed above.
- Provide only short-term training to doctoral-level health professional students through one of the activity codes listed above.
- Receive an award for one or more of the activity codes for doctoral training of graduate students, but do not confer doctoral degrees themselves (e.g., teaching hospitals).
- Receive an institutional training grant award for doctoral training of graduate students from a Public Health Service Agency other than the NIH.

In complying with this Assurance and information disclosure requirement, institutions may decide how best to present the required information to applicants and may wish to consider consolidating data by department or broad program to which candidates apply, or providing additional information in order to provide context.

Grantees with awards for any of the activity codes listed above are also required to provide corresponding information on trainees supported by each of their awards in **Table 12 A - Predoctoral Trainees Supported by this Training Grant** when submitting a renewal application or non-competing continuation progress report (PHS 2590).

2.17 Kirschstein-NRSA Payback Assurance

This is applicable ONLY to the F32 (postdoctoral fellows) and F33 (senior fellows).

Section 487 of the Public Health Service Act, as, amended (42 U.S.C. 288), and implementing regulations (42 CFR part 66) require satisfactory assurance from a prospective recipient of a Kirschstein-NRSA Individual Fellowship that, in the first 12 months of Kirschstein-NRSA postdoctoral support, he or she will meet the following service requirement. Kirschstein-NRSA predoctoral fellows or other fellows who have already had 12 months of Kirschstein-NRSA postdoctoral support do not incur a service payback obligation.

Kirschstein-NRSA Individual Fellowships will be governed by the service payback requirements articulated in the National Research Service Award Guidelines for Individual Awards and Institutional Grants. These guidelines can be found in the NRSA portion of the most recent version of the NIH Grants Policy Statement found at: http://grants.nih.gov/grants/policy/policy.htm#gps. Applicants accepting an approved Kirschstein-NRSA Individual Fellowship agree to the following assurance:

I. Service Requirement - In accepting a Ruth L. Kirschstein National Research Service Award to support my postdoctoral research training, I understand that my first 12 months of Kirschstein-NRSA Individual Fellowship support for postdoctoral research training carry with it a payback obligation. I hereby agree to engage in a month of health-related research, health-related research training, health-related teaching, and/or health-related activities for each month I receive a Kirschstein-NRSA Individual Fellowship for postdoctoral research training up to and including 12 months. If I receive a Kirschstein-NRSA Individual Fellowship for postdoctoral research training for more than 12 months, I agree that the 13th month and each subsequent month of Kirschstein-NRSA-supported postdoctoral research training will satisfy a month of my payback obligation incurred in the first 12

months. This service shall be initiated within 2 years after the end of Kirschstein-NRSA support. The health-related research, teaching, and/or activities shall be on a continuous basis and shall average more than 20 hours per week of a full work year.

II. Financial Payback Provisions - I understand that if I fail to undertake or perform such service in accordance with Section I above, the United States will be entitled to recover from me an amount determined in accordance with the following formula:

$$A = F\,[(t-s)/t]$$

where "A" is the amount the United States is entitled to recover; "F" is the sum of the total amount paid to me under the initial 12 months of my postdoctoral Ruth L. Kirschstein National Research Service Award support; "t" is the total number of months in my service obligation; and "s" is the number of months of such obligation served.

Except as provided in Section III below, any amount the United States is entitled to recover from me shall be paid within the 3-year period beginning on the date the United States becomes entitled to recover such amount. The United States becomes entitled to recover such amount 2 years after termination of my Ruth L. Kirschstein National Research Service Award support if I do not engage in acceptable service payback activities in accordance with Section I. If I elect to engage in financial repayment before the end of the 2-year period, the United States becomes entitled to recover such amount on the date of my election. Interest on the amount begins on the date the United States becomes entitled to recover such amount and is at the rate fixed by the Secretary of the Treasury after taking into consideration private consumer rates prevailing on that date. I understand that I will be allowed an initial 30-day interest-free period in which to fully pay such amount, and that I may prepay any outstanding balance after that period to avoid additional interest. I further understand that I will be subject to authorized debt collection action(s) (including any accrued interest and late fees) should I fail to comply with the payback provisions of this Section II.

III. Conditions for Break in Service, Waiver, and Cancellation - I hereby understand that the Secretary of Health and Human Services:

A. May extend the period for undertaking service, permit breaks in service, or extend the period for repayment, if it is determined that:
    1. Such an extension or break in service is necessary to complete my clinical training or to participate in a NIH Loan Repayment Program;
    2. Completion would be impossible because of temporary disability; or
    3. Completion would involve a substantial hardship and failure to extend such period would be against equity and good conscience;

B. May waive my obligation, in whole or in part, if it is determined that:
    1. Fulfillment would be impossible because I have been permanently or totally disabled; or
    2. Fulfillment would involve a substantial hardship and the enforcement of such obligation would be against equity and good conscience;

C. Will, in the event of my death, cancel any obligation incurred under this payback agreement.

IV. Termination Notice-Annual Report of Employment-Change of Address and/or Name - I agree to complete and submit a termination notice immediately upon completion of support. Thereafter, on an annual basis I agree to complete and submit all Payback Activities Certification forms sent to me by the National Institutes of Health or the Agency for Healthcare Research and Quality concerning post-award activities, and agree to keep those agencies advised of any change of address and/or name until such time as my total obligation is fulfilled.

V. Program Evaluation - I understand that I also may be contacted from time to time, but no more frequently than once every 2 years, after the end of this award to determine how the training obtained has influenced my

career. Any information thus obtained would be used only for statistical purposes and would not identify me individually.

VI. Certification - By signing the certification block on the application form, I certify that I have read and understood the requirements and provisions of this assurance and that I will abide by them if an award is made.

2.18 SBIR Funding Agreement Certification

All small businesses that are selected for award of an SBIR funding agreement must complete a Funding Agreement Certification at the time of award and any other time set forth in the Notice of Award that is prior to performance of work under this award. This includes checking all of the boxes on the actual certification document and having an authorized officer of the awardee sign and date the certification each time it is requested.

The certification is available in fillable format on the SBIR/Forms website: http://grants.nih.gov/grants/forms.htm#sbir. However, the requirements are outlined below.

Overview of Certification Information. The Federal government relies on this information to determine whether the business is eligible for an SBIR Program award. A similar certification will be used to ensure continued compliance with specific program requirements during the life of the funding agreement. The definitions for the terms used in this certification are set forth in the Small Business Act, SBA regulations (13 C.F.R. Part 121), the SBIR Policy Directive and also any statutory and regulatory provisions references in those authorities.

If the Grants Management Officer believes that the business may not meet certain eligibility requirements at the time of award, they are required to file a size protest with the U.S. Small Business Administration (SBA), who will determine eligibility. At that time, SBA will request further clarification and supporting documentation in order to assist in the verification of any of the information provided as part of a protest. If the Grants Management Officer believes, after award, that the business is not meeting certain Notice of Award requirements, the agency may request further clarification and supporting documentation in order to assist in the verification of any of the information provided.

Even if correct information has been included in other materials submitted to the Federal government, any action taken with respect to the certification does not affect the Government's right to pursue criminal, civil, or administrative remedies for incorrect or incomplete information given in the certification. Each person signing the certification may be prosecuted if they have provided false information.

Applicants will verify and certify the following provisions:

1. The business concern meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.
2. If a corporation, all corporate documents (articles of incorporation and any amendments, articles of conversion, by-laws and amendments, shareholder meeting minutes showing director elections, shareholder meeting minutes showing officer elections, organizational meeting minutes, all issued stock certificates, stock ledger, buy-sell agreements, stock transfer agreements, voting agreements, and documents relating to stock options, including the right to convert non-voting stock or debentures into voting stock) evidence that it meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.
3. If a partnership, the partnership agreement evidences that it meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.
4. If a limited liability company, the articles of organization and any amendments, and operating agreements and amendments, evidence that it meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.
5. The birth certificates, naturalization papers, or passports show that any individuals it relies upon to meet the eligibility requirements are U.S. citizens or permanent resident aliens in the United States.
6. It has no more than 500 employees, including the employees of its affiliates.

7. SBA has not issued a size determination currently in effect finding that this business concern exceeds the 500 employee size standard.
8. During the performance of the award, the principal investigator will spend more than half of his/her time as an employee of the awardee or has requested and received a written deviation from this requirement from the Grants Management Officer.
9. All, essentially equivalent work, or a portion of the work proposed under this project. Options on the certification document include:
    - Has not been submitted for funding by another Federal agency
    - Has been submitted for funding by another Federal agency but has not been funded under any other Federal grant, contract, subcontract, or other transaction.
    - A portion has been funded by another grant, contract, or subcontract as described in detail in the proposal and approved in writing by the Grants Management Officer.
10. During the performance of award, it will perform the applicable percentage of work unless a deviation from this requirement is approved in writing by the Grants Management Officer. Options on the certification document include:
    - SBIR Phase I: at least two-thirds (66 2/3%) of the research
    - SBIR Phase II: at least half (50%) of the research
    - Percent deviation approved in writing by the Grants Management Officer
11. During performance of award, the research/research and development will be performed in the United States unless a deviation is approved in writing by the Grants Management Officer.
12. During the performance of award, the research/research and development will be performed at my facilities with my employees, except as otherwise indicated in the SBIR application and approved in the Notice of Award.
13. It has registered itself on SBA's database as majority-owned by venture capital operating companies, hedge funds or private equity firms.
14. It is a Covered Small Business Concern (a small business concern that: (a) was not majority-owned by multiple venture capital operating companies (VCOCs), hedge funds, or private equity firms on the data on which it submitted an application in response to an SBIR solicitation; and (b) on the date of the SBIR award, which is made more than 9 months after the closing date of the solicitation, is majority-owned by multiple venture capital operating companies, hedge funds, or private equity firms).

The applicant will notify the Federal agency immediately if all or a portion of the work proposed is subsequently funded by another Federal agency.

The applicant will further certify that he or she understands that the information submitted may be given to Federal, State and local agencies for determining violations of law and other purposes.

Finally, the individual certifying on behalf of the applicant will certify he or she is:

- An officer of the business concern authorized to represent it and sign this certification on its behalf. By signing this certification
- Representing on his/her own behalf, and on behalf of the business concern that the information provided in the certification, the application, and all other information submitted in connection with the application, is true and correct as of the date of submission.
- Acknowledging that any intentional or negligent misrepresentation of the information contained in the certification may result in criminal, civil or administrative sanctions, including but not limited to
    - fines, restitution and/or imprisonment under 18 U.S.C. § 1001;

- treble damages and civil penalties under the False Claims Act (31 U.S.C. § 3729 et seq);
- double damages and civil penalties under the Program Fraud Civil Remedies Act (31 U.S.C. §3801 et seq);
- civil recovery of award funds;
- suspension and/or debarment from all Federal procurement and nonprocurement transactions (FAR Subpart 9.4 or 2 C.F.R. part 180; and
- other administrative penalties including termination of SBIR/STTR awards.

2.19 STTR Funding Agreement Certification

All small businesses that are selected for award of an STTR funding agreement must complete a Funding Agreement Certification at the time of award and any other time set forth in the Notice of Award that is prior to performance of work under this award. This includes checking all of the boxes on the actual certification document and having an authorized officer of the awardee sign and date the certification each time it is requested.

The certification is available in fillable format on the SBIR/Forms website: http://grants.nih.gov/grants/forms.htm#sbir. However, the requirements are outlined below.

Overview of Certification Information. The Federal government relies on this information to determine whether the business is eligible for an STTR Program award. A similar certification will be used to ensure continued compliance with specific program requirements during the life of the funding agreement. The definitions for the terms used in this certification are set forth in the Small Business Act, SBA regulations (13 C.F.R. Part 121), the SBIR Policy Directive and also any statutory and regulatory provisions references in those authorities.

If the Grants Management Officer believes that the business may not meet certain eligibility requirements at the time of award, they are required to file a size protest with the U.S. Small Business Administration (SBA), who will determine eligibility. At that time, SBA will request further clarification and supporting documentation in order to assist in the verification of any of the information provided as part of a protest. If the Grants Management Officer believes, after award, that the business is not meeting certain funding agreement requirements, the agency may request further clarification and supporting documentation in order to assist in the verification of any of the information provided.

Even if correct information has been included in other materials submitted to the Federal government, any action taken with respect to the certification does not affect the Government's right to pursue criminal, civil, or administrative remedies for incorrect or incomplete information given in the certification. Each person signing the certification may be prosecuted if they have provided false information.

Applicants will verify and certify the following provisions:

1. The business concern meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.
2. If a corporation, all corporate documents (articles of incorporation and any amendments, articles of conversion, by-laws and amendments, shareholder meeting minutes showing director elections, shareholder meeting minutes showing officer elections, organizational meeting minutes, all issued stock certificates, stock ledger, buy-sell agreements, stock transfer agreements, voting agreements, and documents relating to stock options, including the right to convert non-voting stock or debentures into voting stock) evidence that it meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.
3. If a partnership, the partnership agreement evidences that it meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.

4. If a limited liability company, the articles of organization and any amendments, and operating agreements and amendments, evidence that it meets the ownership and control requirements set forth in 13 C.F.R. § 121.702.
5. The birth certificates, naturalization papers, or passports show that any individuals it relies upon to meet the eligibility requirements are U.S. citizens or permanent resident aliens in the United States.
6. It has no more than 500 employees, including the employees of its affiliates.
7. SBA has not issued a size determination currently in effect finding that this business concern exceeds the 500 employee size standard.
8. During the performance of the award, the principal investigator will spend more than half of his/her time as an employee of the awardee or has requested and received a written deviation from this requirement from the Grants Management Officer.
9. All, essentially equivalent work, or a portion of the work proposed under this project. Options on the certification document include:
    - Has not been submitted for funding by another Federal agency
    - Has been submitted for funding by another Federal agency but has not been funded under any other Federal grant, contract, subcontract, or other transaction.
    - A portion has been funded by another grant, contract, or subcontract as described in detail in the proposal and approved in writing by the Grants Management Officer.
10. During the performance of award, it will perform the applicable percentage of work unless a deviation from this requirement is approved in writing by the Grants Management Officer. Options on the certification document include:
    - STTR Phase I: at least forty percent (40%) of the research
    - STTR Phase II: at least forty percent (40%) of the research
    - Percent deviation approved in writing by the Grants Management Officer
11. During performance of award, the research/research and development will be performed in the United States unless a deviation is approved in writing by the Grants Management Officer.
12. During the performance of award, the research/research and development will be performed at my facilities with my employees, except as otherwise indicated in the SBIR application and approved in the Notice of Award.
13. It has registered itself on SBA's database as majority-owned by venture capital operating companies, hedge funds or private equity firms.
14. The small business concern has provided satisfactory evidence that it will exercise management direction and control of the performance of the STTR funding agreement.

The applicant will notify the Federal agency immediately if all or a portion of the work proposed is subsequently funded by another Federal agency.

The applicant will further certify that he or she understands that the information submitted may be given to Federal, State and local agencies for determining violations of law and other purposes.

Finally, the individual certifying on behalf of the applicant will certify he or she is:

- An officer of the business concern authorized to represent it and sign this certification on its behalf.
- Representing on his/her own behalf, and on behalf of the business concern that the information provided in the certification, the application, and all other information submitted in connection with the application, is true and correct as of the date of submission.

- Acknowledging that any intentional or negligent misrepresentation of the information contained in the certification may result in criminal, civil or administrative sanctions, including but not limited to:
    - fines, restitution and/or imprisonment under 18 U.S.C. § 1001;
    - treble damages and civil penalties under the False Claims Act (31 U.S.C. § 3729 et seq);
    - double damages and civil penalties under the Program Fraud Civil Remedies Act (31 U.S.C. §3801 et seq);
    - civil recovery of award funds;
    - suspension and/or debarment from all Federal procurement and nonprocurement transactions (FAR Subpart 9.4 or 2 C.F.R. part 180; and
    - other administrative penalties including termination of SBIR/STTR awards.

2.20 Small Business Concern SBIR VCOC Certification Statement

NIH and CDC SMALL BUSINESS INNOVATION RESEARCH PROGRAM
CERTIFICATION FOR APPLICANTS THAT ARE MAJORITY-OWNED BY MULTIPLE VENTURE CAPITAL OPERATING COMPANIES, HEDGE FUND, OR PRIVATE EQUITY FIRMS

Any small businesses that are majority-owned by multiple venture operating companies (VCOCs), hedge funds or private equity firms and are submitting an application for an SBIR funding agreement must complete a VCOC Certification prior to submitting an application. This includes checking all of the boxes on the actual certification and having an authorized officer of the applicant organization sign and date the certification each time it is requested.

The certification is available in fillable format on the SBIR/Forms website: http://grants.nih.gov/grants/forms.htm#sbir. However, the requirements are outlined below.

Overview of Certification Information. The Federal government relies on the information to determine whether the business is eligible for an SBIR Program award and meets the specific program requirements during the life of the funding agreement. The definitions for the terms used in this certification are set forth in the Small Business Act, SBA regulations (13 C.F.R. Part 121), the SBIR Policy Directive and also any statutory and regulatory provisions referenced in those authorities.

If the funding agreement officer believes that the business may not meet certain eligibility requirements at the time of award, they are required to file a size protest with the U.S. Small Business Administration (SBA), who will determine eligibility. At that time, SBA will request further clarification and supporting documentation in order to assist in the verification of any of the information provided as part of a protest. If the funding agreement officer believes, after award, that the business is not meeting certain funding agreement requirements, the agency may request further clarification and supporting documentation in order to assist in the verification of any of the information provided.

Even if correct information has been included in other materials submitted to the Federal government, any action taken with respect to the certification does not affect the Government's right to pursue criminal, civil or administrative remedies for incorrect or incomplete information given in the certification. Each person signing the certification may be prosecuted if they have provided false information.

Applicants will verify and certify the following provisions:

1. The applicant is NOT more than 50% owned by a single VCOC, hedge fund or private equity firm.
2. The applicant is more than 50% owned by multiple domestic business concerns that are VCOCs, hedge funds, or private equity firms.
3. I have registered with SBA at www.SBIR.gov as a business that is majority-owned by multiple VCOCs, hedge funds or private equity firms.

The applicant will further certify that they understand that the information submitted may be given to Federal, State and local agencies for determining violations of law and other purposes.

- All the statements and information provided in the certification and any documents submitted are true, accurate and complete. If assistance was obtained in completing the certification and the supporting documentation, the certifying official has personally reviewed the information and it is true and accurate. The certifying official understands that, in general, these statements are made for the purpose of determining eligibility for an SBIR funding agreement and continuing eligibility.
- The certifying official understands that the certifications in the document are continuing in nature. Each SBIR funding agreement for which the small business submits an offer or application or receives an award constitutes a restatement and reaffirmation of these certifications.
- The certifying official understands that he/she may not misrepresent status as small business to: (1) obtain a contract under the Small Business Act; or (2) obtain any benefit under a provision of Federal law that references the SBIR Program.

Finally, the individual certifying on behalf of the grantee will certify they are:

- An officer of the business concern authorized to represent it and sign this certification on its behalf.
- Representing on his/her own behalf, and on behalf of the SBIR applicant or awardee, that the information provided in this the certification, the application, and all other information submitted in connection with this the application, is true and correct as of the date of submission.
- Acknowledging that any intentional or negligent misrepresentation of the information contained in this certification may result in criminal, civil or administrative sanctions, including but not limited to:
    - fines, restitution and/or imprisonment under 18 U.S.C. §1001;
    - treble damages and civil penalties under the False Claims Act (31 U.S.C. §3729 et seq.);
    - double damages and civil penalties under the Program Fraud Civil Remedies Act (31 U.S.C. §3801 et seq.);
    - civil recovery of award funds;
    - suspension and/or debarment from all Federal procurement and nonprocurement transactions (FAR Subpart 9.4 or 2 C.F.R. part 180); and
    - other administrative penalties including termination of SBIR/STTR awards.

3. Definitions

Activity Code. A 3-character code used to identify a specific category of extramural research activity, applied to various funding activity codes. NIH uses three funding activity codes for extramural research awards: grants, cooperative agreements, and contracts. Within each funding activity code, NIH uses 3-character activity codes (e.g., F32, K08, P01, R01, T32, etc.) to differentiate the wide variety of research-related programs NIH supports. A comprehensive list of activity codes is on the NIH Web site at http://grants.nih.gov/grants/funding/ac_search_results.htm.

AHRQ. Agency for Healthcare Research and Quality, which is a component of HHS.

AIDS Related. Includes: (1) projects relating to the etiology, epidemiology, natural history, diagnosis, treatment, or prevention of AIDS; (2) various sequelae specifically associated with the syndrome; and (3) preparation and screening of anti-AIDS agents as well as vaccine development, including both preclinical and clinical studies. Not all applications examining various influences on T-lymphocytes or retroviruses will be appropriate for the expedited AIDS review process. Applications only indirectly related to AIDS will be evaluated by established Scientific Review Groups (SRGs) appropriate to the scientific discipline during regular NIH review cycles and should not be submitted in response to the expedited AIDS receipt dates. Applicants are

urged to take note of the yearly NIH Plan for HIV-Related Research and indicate how their application addresses the NIH priorities set forth in that Plan. The Plan can be found on the NIH Office of AIDS Research homepage.

Affiliate. This term has the same meaning as set forth in 13 CFR part 121 – Small Business Size Regulations, §121.103, "How does SBA determine affliliation?" Further information about SBA's affiliation rules and a guide on affiliation is available at http://www.SBIR.gov and http://www.SBA.gov/size.

Animal. Any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes. The generation of custom antibodies constitutes an activity involving vertebrate animals.

Applicant. For purposes of the SBIR/STTR programs, the organizational entity that, at the time of award, will qualify as a Small Business Concern (SBC) and that submits a grant application for a funding agreement under the SBIR or STTR program.

Applicant Organization Types.

Federal: A cabinet-level department or independent agency of the Executive Branch of the Federal Government or any component part of such a department or agency that may be assigned the responsibility for carrying out a grant-supported program.

State: Any agency or instrumentality of a state government of any of the United States or its territories.

Local: Any agency or instrumentality of a political subdivision of government below the State level.

Nonprofit: An institution, corporation, or other legal entity no part of whose net earnings may lawfully inure to the benefit of any private shareholder or individual.

For profit: An institution, corporation, or other legal entity, which is organized for the profit or benefit of its shareholders or other owners. A "for profit" organization is considered to be a small business if it is independently owned and operated, if it is not dominant in the field in which research is proposed, and if it employs no more than 500 persons. Also see definition for Small Business Concern.

Small Business Concern: For purposes of the SBIR/STTR programs, a concern that, on the date of award for both Phase I and Phase II funding agreements:

SBIR PROGRAM

For SBIR FOAs issued prior to January 28, 2013:

Only United States small business concerns (SBCs) are eligible to submit SBIR applications. A small business concern is one that, on the date of award for both Phase I and Phase II funding agreements:

1. Is organized for profit, with a place of business located in the United States, which operates primarily within the United States or which makes a significant contribution to the United States economy through payment of taxes or use of American products, materials or labor;
2. Is in the legal form of an individual proprietorship, partnership, limited liability company, corporation, joint venture, association, trust or cooperative, except that where the form is a joint venture, there can be no more than 49 percent participation by foreign business entities in the joint venture;
3. Is at least 51 percent owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States, except in the case of a joint venture, where each entity to the venture must be 51 percent owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States; and
4. Has, including its affiliates, not more than 500 employees.

For SBIR FOAs issued after January 28, 2013:

Only United States small business concerns (SBCs) are eligible to submit applications for this opportunity. A small business concern is one that, at the time of award of Phase I and Phase II, meets *all* of the following criteria:

1. Is organized for profit, with a place of business located in the United States, which operates primarily within the United States or which makes a significant contribution to the United States economy through payment of taxes or use of American products, materials or labor;
2. Is in the legal form of an individual proprietorship, partnership, limited liability company, corporation, joint venture, association, trust or cooperative, except that where the form is a joint venture, there must be less than 50 percent participation by foreign business entities in the joint venture;
3. (i) Be a concern which is more than 50% directly owned and controlled by one or more individuals (who are citizens or permanent resident aliens of the United States), other business concerns (each of which is more than 50% directly owned and controlled by individuals who are citizens or permanent resident aliens of the United States), or any combination of these; OR

   (ii) **NIH and CDC only.** Be a concern which is more than 50% owned by multiple venture capital operating companies, hedge funds, private equity firms, or any combination of these. No single venture capital operating company, hedge fund, or private equity firm may own more than 50% of the concern; OR

   (iii) Be a joint venture in which each entity to the joint venture must meet the requirements set forth in paragraph 3 (i) or 3 (ii) of this section. A joint venture that includes one or more concerns that meet the requirements of paragraph (ii) of this section must comply with § 121.705(b) concerning registration and proposal requirements.
4. Has, including its affiliates, not more than 500 employees.

NIH and CDC only. If the concern is more than 50% owned by multiple venture capital operating companies, hedge funds, private equity firms, or any combination of these falls under 3 (ii) or 3 (iii) above, see Section IV. Application and Submission Information in the SBIR FOA for additional instructions regarding required application certification.

See Section 4.4 Other Project Information Form instructions in the SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies for additional requirements for small business concerns that are more than 50% owned by multiple venture capital operating companies, hedge funds, private equity firms.

STTR PROGRAM

For STTR FOAs issued prior to January 28, 2013:

Only United States small business concerns (SBCs) are eligible to submit STTR applications. A small business concern is one that, on the date of award for both Phase I and Phase II funding agreements:

1. Is organized for profit, with a place of business located in the United States, which operates primarily within the United States or which makes a significant contribution to the United States economy through payment of taxes or use of American products, materials or labor;
2. Is in the legal form of an individual proprietorship, partnership, limited liability company, corporation, joint venture, association, trust or cooperative, except that where the form is a joint venture, there can be no more than 49 percent participation by foreign business entities in the joint venture;
3. Is at least 51 percent owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States, except in the case of a joint venture, where each

entity to the venture must be 51 percent owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States; and

4. Has, including its affiliates, not more than 500 employees.

For STTR FOAs issued after January 28, 2013:

Only United States small business concerns (SBCs) are eligible to submit applications for this opportunity. A small business concern is one that, at the time of award of Phase I and Phase II, meets *all* of the following criteria:

1. Is organized for profit, with a place of business located in the United States, which operates primarily within the United States or which makes a significant contribution to the United States economy through payment of taxes or use of American products, materials or labor;
2. Is in the legal form of an individual proprietorship, partnership, limited liability company, corporation, joint venture, association, trust or cooperative, except that where the form is a joint venture, there must be less than 50 percent participation by foreign business entities in the joint venture;
3. (i) Be a concern which is more than 50% directly owned and controlled by one or more individuals (who are citizens or permanent resident aliens of the United States), other business concerns (each of which is more than 50% directly owned and controlled by individuals who are citizens or permanent resident aliens of the United States), or any combination of these; OR
   (ii) Be a joint venture in which each entity to the joint venture must meet the requirements set forth in paragraph 3 (i) of this section. A joint venture that includes one or more concerns that meet the requirements of paragraph (ii) of this section must comply with § 121.705(b) concerning registration and proposal requirements.
4. Has, including its affiliates, not more than 500 employees.

Control can be exercised through common ownership, common management, and contractual relationships. The term "affiliates" is defined in greater detail in 13 CFR part 121, as is the process for calculating "number of employees."

Business concerns include, but are not limited to, any individual (sole proprietorship), partnership, corporation, joint venture, association, or cooperative. Further information may be obtained by contacting the Small Business Administration Size District Office at http://www.sba.gov/size/.

Socially and Economically Disadvantaged Small Business Concern: See 13 CFR part 124, Subpart B. A socially and economically disadvantaged small business concern is one that is at least 51% owned by (a) an Indian tribe or a native Hawaiian organization, or (b) one or more socially and economically disadvantaged individuals; **and** whose management and daily business operations are controlled by one or more socially and economically disadvantaged individuals.

Women-Owned Small Business Concern: An SBC that is at least 51% owned by one or more women, or in the case of any publicly owned business, at least 51% of the stock is owned by women, and women control the management and daily business operations.

Catalog of Federal Domestic Assistance (CFDA) number. Catalog of Federal Domestic Assistance (CFDA) number.

CFDA program title. CFDA program title means the title of the program under which the Federal award was funded in the CFDA.

CFR. Code of Federal Regulations.

Clinical Research. See Human Subjects Research Definitions and Terms.

Clinical Trial. See Human Subjects Research Definitions and Terms.

Coded. See Human Subjects Research Definitions and Terms

Co-Investigator. An individual involved with the PD/PI in the scientific development or execution of a project. The co-investigator (collaborator) may be employed by, or be affiliated with, the applicant/grantee organization or another organization participating in the project under a consortium agreement. A co-investigator typically devotes a specified percent of effort to the project and is considered senior/key personnel. The designation of a co-investigator, if applicable, does not affect the PD/PI's roles and responsibilities as specified in the *NIH Grants Policy Statement*.

Collaborator. An individual involved with the PD/PI in the scientific development or execution of the project. These individuals would typically devote a specific percent of effort to the project and would be identified as senior/key personnel. The collaborator may be employed by, or affiliated with, either the grantee organization or an organization participating in the project under a consortium or contractual agreement.

Component. For the purposes of applications and progress reports, a component is a distinct, reviewable part of a multi-project application or progress report for which there is a business need to gather detailed information identified in the funding opportunity announcement (FOA). Components typically include general information (component organization, project period, project title, etc.), performance sites, personnel, and budget. The FOA defines the construction and naming convention for the application; the funded application defines the construction and naming convention for the progress report. Components may also be referred to as "cores" or "projects." Note, for RPPR Question G.9, the term "foreign component" is distinct from "component" as defined here. However, a "foreign component" may also be a "component" in the RPPR. (See definition of foreign component for more information.)

Commercialization. The process of developing products, processes, technologies, or services and the production and delivery (whether by the originating party or others) of the products, processes, technologies, or services for sale to or use by the Federal government or commercial markets.

Computing devices. Computing devices means machines used to acquire, store, analyze, process, and publish data and other information electronically, including accessories (or ''peripherals'') for printing, transmitting and receiving, or storing electronic information. See also 200.94 Supplies and 200.58 Information technology systems.

Consortium Agreement. A formalized agreement whereby a research project is carried out by the grantee and one or more other organizations that are separate legal entities. Under the agreement, the grantee must perform a substantive role in the conduct of the planned research and not merely serve as a conduit of funds to another party or parties. These agreements typically involve a specific percent of effort from the consortium organization's PD/PI and a categorical breakdown of costs, such as personnel, supplies, and other allowable expenses, including Facilities and Administrative costs.

Consultant. An individual who provides professional advice or services for a fee, but normally not as an employee of the engaging party. In unusual situations, an individual may be both a consultant and an employee of the same party, receiving compensation for some services as a consultant and for other work as a salaried employee. To prevent apparent or actual conflicts of interest, grantees and consultants must establish written guidelines indicating the conditions of payment of consulting fees. Consultants may also include firms that provide paid professional advice or services.

Consulting Fees. The fee paid by an institution to a salaried member of its faculty is allowable only in unusual cases and only if both of the following conditions exist: (1) the consultation crosses departmental lines or involves a separate operation; and (2) the work performed by the consultant is in addition to his or her regular workload.

In all other cases, consulting fees paid to employees of recipient or cost-type contractor organizations in addition to salary may be charged to PHS grant-supported projects only in unusual situations and when all of the following conditions exist: (1) the policies of the recipient or contractor permit such consulting fee payments to its own employees regardless of whether Federal grant funds are received; (2) the consulting services are clearly outside the scope of the individual's salaried employment; and (3) it would be inappropriate or not feasible to compensate the individual for these services through payment of additional salary.

For additional clarification on the allowance and appropriateness of consulting fees, refer to the *NIH Grants Policy Statement*.

Contract. Contract means a legal instrument by which a non-Federal entity purchases property or services needed to carry out the project or program under a Federal award. The term does not include a legal instrument, even if the non-Federal entity considers it a contract, when the substance of the transaction meets the definition of a Federal award or subaward.

Contractor. Contractor means an entity that receives a contract as defined in Contract.

Cooperative Agreement. Cooperative agreement means a legal instrument of financial assistance between a Federal awarding agency or pass-through entity and a non-Federal entity that, consistent with 31 U.S.C. 6302–6305: (a) Is used to enter into a relationship the principal purpose of which is to transfer anything of value from the Federal awarding agency or pass through entity to the non-Federal entity to carry out a public purpose authorized by a law of the United States (see 31 U.S.C. 6101(3)); and not to acquire property or services for the Federal government or pass-through entity's direct benefit or use; (b) Is distinguished from a grant in that it provides for substantial involvement between the Federal awarding agency or pass-through entity and the non-Federal entity in carrying out the activity contemplated by the Federal award. (c) The term does not include: development agreement as defined in 15 U.S.C. 3710a; or (2) An agreement that provides only: (i) Direct United States Government cash assistance to an individual; (ii) A subsidy; (iii) A loan; (iv) A loan guarantee; or (v) Insurance.

Covered Small Business Concern. For purposes of the SBIR/STTR programs, a small business concern that:

1. Was not majority-owned by multiple venture capital operating companies (VCOCs), hedge funds, or private equity firms on the date on which it submitted an application in response to a solicitation under the SBIR program; and
2. Is majority-owned by multiple venture capital operating companies, hedge funds, or private equity firms on the date of the SBIR award.

Data Universal Numbering System (DUNS) number. DUNS number means the nine-digit number established and assigned by Dun and Bradstreet, Inc. (D&B) to uniquely identify entities. A non-Federal entity is required to have a DUNS number in order to apply for, receive, and report on a Federal award. A DUNS number may be obtained from D&B by telephone (currently 866–705–5711) or the Internet (currently at http://fedgov.dnb.com/webform).

Early Stage Investigator. An individual who qualifies as a New Investigator and is within 10 years of completing his/her terminal research degree or is within 10 years of completing medical residency (or the equivalent). See NOT-OD-09-034 for information concerning an extension of ESI status.

Employees. The number of employees of a firm is its average number of persons employed for each pay period over the firm's latest 12 months. Any person on the payroll must be included as one employee regardless of hours worked or temporary status. The number of employees of a firm in business under 12 months is based on the average for each pay period it has been in business.

Equipment. An article of tangible, nonexpendable, personal property having a useful life of more than one year and an acquisition cost of $5,000 or more, or the capitalization threshold established by the organization, whichever is less.

Essentially Equivalent Work. This term is meant to identify "scientific overlap," which occurs when (1) substantially the same research is proposed for funding in more than one contract proposal or grant application submitted to the same Federal agency; **or** (2) substantially the same research is submitted to two or more different Federal agencies for review and funding consideration; **or** (3) a specific research objective and the research design for accomplishing that objective are the same or closely related in two or more proposals or awards, regardless of the funding source.

Expanded Authorities/NIH Standard Terms of Award. The operating authorities provided to grantees under certain research grant mechanisms that waive the requirement for NIH prior approval for specified actions. NIH

extended expanded authorities to all NIH awards except for the provision to automatically carry over unobligated balances thus these authorities have become the NIH Standard Terms of Award. Therefore, the term Expanded Authorities is no longer used at NIH. See the NIH Grants Policy Statement (standard terms of award in chapter 8) and the NIH Guide Notice (http://grants.nih.gov/grants/ guide/notice-files/NOT-OD-01-070.html) which expanded the authorities (other than Phase I carry-over) to include Phase I SBIR/STTR.

Facilities and Administrative (Indirect) Costs. Facilities and Administrative (F&A) Costs are defined as costs that are incurred by a grantee for common or joint objectives and that, therefore, cannot be identified specifically with a particular project or program.

Feasibility. The extent to which a study or project may be done practically and successfully.

Federal agency. Federal agency means an ‘‘agency’’ as defined at 5 U.S.C. 551(1) and further clarified by 5 U.S.C. 552(f).

Federal awarding agency. Federal awarding agency means the Federal agency that provides a Federal award directly to a non-Federal entity.

Federal Award Identification Number. A unique number assigned to a financial assistance award to assist recipients in correctly reporting subawards. The public can use the FAIN and the CFDA number together to find one accurate result when searching on line in such databases as USASpending.gov and FSRS. The FAIN can be found on the notice of award. NIH implements the FAIN by deriving it from the core elements of the grant number. For example, the FAIN for 1R0lGM654321-01 would be R01GM654321.

Federal Laboratory. As defined in 15 U.S.C. §3703, means any laboratory, any federally funded research and development center, or any center established under 15 U.S.C. §§ 3705 & 3707 that is owned, leased, or otherwise used by a Federal agency and funded by the Federal Government, whether operated by the Government or by a contractor.

Foreign Component. The performance of any significant scientific element or segment of a project outside of the United States, either by the grantee or by a researcher employed by a foreign organization, whether or not grant funds are expended. Activities that would meet this definition include, but are not limited to, (1) the involvement of human subjects or animals; (2) extensive foreign travel by grantee project staff for the purpose of data collection, surveying, sampling, and similar activities; or (3) any activity of the grantee that may have an impact on U.S. foreign policy through involvement in the affairs or environment of a foreign country. Examples of other grant-related activities that may be significant are: collaborations with investigators at a foreign site anticipated to result in co-authorship; use of facilities or instrumentation at a foreign site; or receipt of financial support or resources from a foreign entity. Foreign travel for consultation is not considered a foreign component.

Foreign organization. Foreign organization means an entity that is: (a) A public or private organization located in a country other than the United States and its territories that are subject to the laws of the country in which it is located, irrespective of the citizenship of project staff or place of performance; (b) A private nongovernmental organization located in a country other than the United States that solicits and receives cash contributions from the general public; (c) A charitable organization located in a country other than the United States that is nonprofit and tax exempt under the laws of its country of domicile and operation, and is not a university, college, accredited degree granting institution of education, private foundation, hospital, organization engaged exclusively in research or scientific activities, church, synagogue, mosque or other similar entities organized primarily for religious purposes; or (d) An organization located in a country other than the United States not recognized as a Foreign Public Entity.

Full-Time Appointment. The number of days per week and/or months per year representing full-time effort at the applicant/grantee organization, as specified in organizational policy. The organization's policy must be applied consistently regardless of the source of support.

General purpose equipment. General purpose equipment means equipment which is not limited to research, medical, scientific or other technical activities. Examples include office equipment and furnishings, modular offices, telephone networks, information technology equipment and systems, air conditioning equipment, reproduction and printing equipment, and motor vehicles. See also Equipment and Special Purpose Equipment.

Grant. A financial assistance mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity. A grant is used whenever the NIH Institute or Center anticipates no substantial programmatic involvement with the recipient during performance of the financially assisted activities.

Grantee. The organization or individual awarded a grant or cooperative agreement by NIH that is responsible and accountable for the use of the funds provided and for the performance of the grant-supported project or activity. The grantee is the entire legal entity even if a particular component is designated in NoA. The grantee is legally responsible and accountable to NIH for the performance and financial aspects of the grant-supported project or activity. Also known as awardee or recipient.

HHS. U.S. Department of Health and Human Services.

Hedge Fund. For purposes of the SBIR/STTR programs, hedge fund has the meaning given that term in section 13(h)(2) of the Bank Holding Company Act of 1956 (12 U.S.C. 1851(h)(2)). The hedge fund must have a place of business located in the United States and be created or organized in the United States, or under the law of the United States or of any State.

Historically Underutilized Business Zone (HUBZone). A small business concern meeting the following criteria:

1. Located in a "historically underutilized business zone" or HUBZone area located in one or more of the following:
    1. A qualified census tract (as defined in section 42(d)(5)(C)(i)(l) of the Internal Revenue Code of 1986; or
    2. A qualified "non-metropolitan county" (as defined in section 143(k)(2)(B) of the Internal Revenue Code of 1986) with a median household income of less than 80 percent of the state median household income or with an unemployment rate of not less than 140 percent of the statewide average, based on U.S. Department of Labor recent data; or
    3. Lands within the boundaries of Federally recognized Indian reservations.
2. Owned and controlled by one or more U.S. Citizens.
3. At least 35% of its employees must reside in a HUBZone.

Human Subjects Research Definitions and Terms.

Autopsy Materials. The use of autopsy materials is governed by applicable federal, state and local law and is not directly regulated by 45 CFR part 46.

Child. The NIH Policy on Inclusion of Children now defines a child as an individual under the age of 18 years. The intent of the NIH policy is to provide the opportunity for children to participate in research studies when there is a sound scientific rationale for including them, and their participation benefits children and is appropriate under existing Federal guidelines. Thus, children must be included in NIH conducted or supported clinical research unless there are scientific or ethical reasons not to include them.

HHS Regulations (45 CFR part 46, Subpart D, Sec.401-409) provide additional protections for children involved as subjects in research, based on this definition: "Children are persons who have not attained the legal age for consent to treatments or procedures involved in research, under the applicable law of the jurisdiction in which the research will be conducted." Generally, state laws define what constitutes a "child." Consequently, the age at which a child's own consent is required and sufficient to participate in research will vary according to state law. For example, some states consider a person age 18 to be an adult and therefore one who can provide consent without parental permission.

Clinical Research. NIH defines human clinical research as research with human subjects that is: (1) Patient-oriented research. Research 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, or (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research. Note: Studies falling under Exemption 4 for human subjects research are not considered clinical research by this definition.

Clinical Trial. The NIH defines a *clinical trial* as a research study[1] in which one or more human subjects[2] are prospectively assigned[3] to one or more interventions[4] (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes[5].

[1]See Common Rule definition of research at 45 CFR 46.102(d).

[2]See Common Rule definition of human subject at 45 CFR 46.102(f).

[3]The term "prospectively assigned" refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

[4]An intervention is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

[5]Health-related biomedical or behavioral outcome is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status, or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

For additional information see NOT-OD-15-015

NIH-Defined Phase III Clinical Trial. An NIH-defined Phase III clinical trial is a broadly based prospective Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or controlled intervention or comparing two or more existing treatments. Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included.

Coded. With respect to private information or human biological specimens, *coded* means that:

- identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol or combination thereof (i.e., the code); and
- a key to decipher the code exists, enabling linkage of the identifying information with the private information or specimens.

Research that involves only coded private information/data or coded human biological specimens may not constitute human subjects research under the HHS human subjects regulations (45 CFR 46) if:

- the specimens and/or information/data are not obtained from an interaction/intervention with the subject specifically for the research; and
- the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain (e.g., the researcher's access to subject identities is prohibited).

Individuals who provide coded information or specimens for proposed research and who also collaborate on the research involving such information or specimens are considered to be involved in the conduct of human subjects research.

(See the following guidance from the Office for Human Research Protections (OHRP) for additional information and examples: http://www.hhs.gov/ohrp/policy/cdebiol.html.)

Data and Safety Monitoring Plan. For each clinical trial (See definition of "clinical trial" under Part III.3), NIH requires a data and safety monitoring plan that will provide oversight and monitoring to ensure the safety of participants and the validity and integrity of the data. The level of monitoring should be commensurate with the risks and the size and complexity of the clinical trial. A detailed data and safety monitoring plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects. The reporting of Adverse Events must be reported to the IRB, the DSMB (if applicable), the NIH funding Institute or Center, and other required entities. This policy requirement is in addition to any monitoring requirements imposed by 45 CFR part 46.

Data and Safety Monitoring Board (DSMB). NIH requires the establishment of a Data and Safety Monitoring Board (DSMB) for multi-site clinical trials involving interventions that entail potential risk to the participants, *and generally for Phase III clinical trials*. A DSMB also may be appropriate for clinical trials if the studies are blinded (masked), employ high-risk interventions, or involve vulnerable populations.

Exemptions. The six categories of research exempt from the HHS human subject regulations are:

Exemption 1: Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exemption 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:

(i) information obtained is recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

Exemption 2 for research involving survey or interview procedures or observation of public behavior, does not apply to research with children (see **45 CFR part 46, Subpart D**), except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Exemption 3: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Exemption 4: Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the

information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

The humans subjects regulations decision charts (http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html) of the Office for Human Research Protection (OHRP) will determine whether the research falls under the human subjects regulations and if so, whether it meets the criteria for Exemption 4. The NIH Office of Extramural Research Web site also contains information that is helpful for determining whether human subjects research meets the criteria for Exemption 4. See http://grants.nih.gov/grants/policy/hs/index.htm.

Research that meets the criteria for Exemption 4 is not considered "clinical research" as defined by NIH. Therefore, the NIH policies for inclusion of women, minorities, and children in clinical research, and planned enrollment reports, do not apply to research projects covered by Exemption 4.

Exemption 5: Research and demonstration projects that are conducted by or subject to the approval of Department or Agency heads and that are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs (ii) procedures for obtaining benefits or services under those programs (iii) possible changes in or alternatives to those programs or procedures or (iv) possible changes in methods or levels of payment for benefits or services under those programs. Note: It is uncommon for investigators applying for an NIH grant to qualify for this exemption. Please see guidance from the relevant NIH IC or from the OER Human Subjects Protections staff if you think your project is eligible for Exemption 5.

Exemption 6: Taste and food quality evaluation and consumer acceptance studies (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Human Subjects **Exemptions** do **not** apply to research involving prisoners or subjects who become prisoners (see **Subpart C**).

Human Subjects. The HHS regulations "Protection of Human Subjects" (45 CFR 46, administered by OHRP) define a ***human subject*** as a living individual about whom an *investigator* conducting *research obtains*:

- data through intervention or interaction with the individual or
- identifiable private information.

Italicized words and phrases in the definition of human subjects are defined as follows:

Investigator. The OHRP considers the term investigator to include anyone involved in conducting the research. OHRP does not consider the act of solely providing coded private information or specimens (for example, by a tissue repository) to constitute involvement in the conduct of the research. However, if the individuals who provide *coded* information or specimens also collaborate on other activities related to the conduct of the research with the investigators who receive such information or specimens, they will be considered to be involved in the conduct of the research. (See OHRP's Guidance on Research Involving Coded Private Information or Biological Specimens: http://www.hhs.gov/ohrp/policy/cdebiol.html.)

Research. HHS regulations define *research* at 45 CFR 46.102(d) as follows:
Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or

supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Obtains. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:

(a) observing or recording private behavior;

(b) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided to investigators from any source; and

(c) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. (45 CFR 46.102(f))

Interaction includes communication or interpersonal contact between investigator and subject. (45 CFR 46.102(f))

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record). Private information must be *individually identifiable* (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. (45 CFR 46.102(f))

Individually Identifiable Private Information. According to its guidance for use of coded specimens, OHRP generally considers private information or specimens to be *individually identifiable* as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through *coding* systems. Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Sex/Gender. Refers to the classification of research subjects into two categories: male and female. In some cases, representation is unknown, because sex/gender composition cannot be accurately determined (e.g., pooled blood samples or stored specimens without sex/gender designation). In addition, sex/gender classification is based on the self-reporting of participants enrolled in the research study. Investigators should consider the scientific goals of their study when requesting this information particularly if the research may include individuals whose gender identity differs from their sex assigned at birth.

Significant Difference. For purposes of NIH policy, a "significant difference" is a difference that is of clinical or public health importance, based on substantial scientific data. This definition differs from the commonly used "statistically significant difference," which refers to the event that, for a given set of data, the statistical test for a difference between the effects in two groups achieves statistical significance. Statistical significance depends upon the amount of information in the data set. With a very large amount of information, one could find a statistically significant, but clinically small difference that is of very little clinical importance. Conversely, with less information one could find a large difference of potential importance that is not statistically significant.

Valid Analysis. This term means an unbiased assessment. Such an assessment will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect. The principal requirements for ensuring a valid analysis of the question of interest are: allocation of study participants of both

sexes/genders (males and females) and from different racial and/or ethnic groups to the intervention and control groups by an unbiased process such as randomization; unbiased evaluation of the outcome(s) of study participants; and use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects by sex/gender, race, and/or ethnicity.

IC. An Institute or Center of the National Institutes of Health.

Indirect (facilities & administrative (F&A)) costs. Indirect (F&A) costs means those costs incurred for a common or joint purpose benefitting more than one cost objective, and not readily assignable to the cost objectives specifically benefitted, without effort disproportionate to the results achieved. To facilitate equitable distribution of indirect expenses to the cost objectives served, it may be necessary to establish a number of pools of indirect (F&A) costs. Indirect (F&A) cost pools should be distributed to benefitted cost objectives on bases that will produce an equitable result in consideration of relative benefits derived.

HHS: Indirect (Facilities and Administration or F&A) costs means necessary costs incurred by a recipient for a common or joint purpose benefitting more than one cost objective, and not readily assignable to the cost objectives specifically benefitted, without effort disproportionate to the results achieved. To facilitate equitable distribution of indirect expenses to the cost objectives served, it may be necessary to establish a number of pools of indirect (F&A) costs. Indirect (F&A) cost pools should be distributed to benefitted cost objectives on bases that will produce an equitable result in consideration of relative benefits derived.

Information technology systems. Information technology systems means computing devices, ancillary equipment, software, firmware, and similar procedures, services (including support services), and related resources.

Innovation. Something new or improved, including research for (1) development of new technologies, (2) refinement of existing technologies, or (3) development of new applications for existing technologies. For the purposes of PHS programs, an example of "innovation" would be new medical or biological products for improved value, efficiency, or costs.

Institutional Animal Care and Use Committee (IACUC). An administrative body established to oversee the institution's animal program, facilities and research activities.

Institutional Base Salary. The annual compensation paid by an organization for an employee's appointment, whether that individual's time is spent on research, teaching, patient care, or other activities. Base salary excludes any income that an individual may be permitted to earn outside of duties for the applicant/grantee organization. Base salary may not be increased as a result of replacing organization salary funds with NIH grant funds.

Some PHS grant programs are currently subject to a legislatively imposed salary limitation. Any adjustment for salary limits will be made at time of award. Applicants are encouraged to contact their offices of sponsored programs or see the *NIH Guide for Grants and Contracts* for current guidance on salary requirements.

Institutional Review Board (IRB). An administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities.

Institutions of Higher Education (IHEs). IHE is defined at 20 U.S.C. 1001**.**

Intangible property. Property that does not have physical existence. The term includes copyrights, patents, and other intellectual property generated or developed under awards. It also includes copyrights for which assignments of rights are acquired under awards; patents and other intellectual property for which ownership is acquired under awards; loans, notes, and other debt instruments (even if considered tangible for some purposes); lease agreements; and stock and other instruments of property ownership.

Intellectual Property. The separate and distinct types of intangible property that are referred to collectively as "intellectual property," including but not limited to: patents, trademarks, copyrights, trade secrets, SBIR/STTR technical data (as defined in this section), ideas, designs, know-how, business, technical and research methods, and other types of intangible business assets, and including all types of intangible assets either proposed or generated by an SBC as a result of its participation in the SBIR program.

Internal controls. Internal controls means a process, implemented by a non-Federal entity, designed to provide reasonable assurance regarding the achievement of objectives in the following categories: (a) Effectiveness and efficiency of operations; (b) Reliability of reporting for internal and external use; and (c) Compliance with applicable laws and regulations.

IRB Authorization Agreement. A formal, written document that details an agreement for an institution engaged in nonexempt human subjects research to rely on the institutional review board (IRB) of another institution.

Joint Venture. An association of concerns with interests in any degree or proportion by way of contract, express or implied, consorting to engage in and carry out a single specific business venture for joint profit, for which purpose they combine their efforts, property, money, skill, or knowledge, but not on a continuing or permanent basis for conducting business generally. A joint venture is viewed as a business entity in determining power to control its management. See 13 C.F.R. §121.103(h).

Key Biological and/or Chemical Resources. Key biological and/or chemical resources may or may not be generated with NIH funds and: 1) may differ from laboratory to laboratory or over time; 2) may have qualities and/or qualifications that could influence the research data; and 3) are integral to the proposed research. These include, but are not limited to, cell lines, specialty chemicals, antibodies, and other biologics.

Local government. Local government means any unit of government within a state, including a: (a) County; (b) Borough; (c) Municipality; (d) City; (e) Town; (f) Township; (g) Parish; (h) Local public authority, including any public housing agency under the United States Housing Act of 1937; (i) Special district; (j) School district; (k) Intrastate district; (l) Council of governments, whether or not incorporated as a nonprofit corporation under state law; and (m) Any other agency or instrumentality of a multi-, regional, or intra-state or local government.

Market Research. For purposes of the SBIR/STTR programs, "market research" is defined as the systematic gathering, editing, recording, computing, ad analyzing of data about problems related to the sale and distribution of the subject of the research project. It includes various types of research, such as the size of potential market and potential sales volume, the identification of consumers most apt to purchase the product(s), and the advertising media most likely to stimulate their purchases. However, "market research" does NOT include activities under a research plan or protocol that require a survey of the public as part of the objective of the project to determine the impact of the subject of the research on the behavior of individuals.

Mechanisms. Extramural research awards are divided into three main funding activity mechanisms: grants, cooperative agreements and contracts. A funding mechanism is the type of funded application or transaction used at the NIH. Programs are areas within the funding mechanisms. Activity codes identify categories applied to the various funding mechanisms. Also known as award mechanism or support mechanism.

Modified Total Direct Cost (MTDC). MTDC means all direct salaries and wages, applicable fringe benefits, materials and supplies, services, travel, and subawards and subcontracts up to the first $25,000 of each subaward or subcontract (regardless of the period of performance of the subawards and subcontracts under the award). MTDC excludes equipment, capital expenditures, charges for patient care, rental costs, tuition remission, scholarships and fellowships, participant support costs and the portion of each subaward and subcontract in excess of $25,000. Other items may only be excluded when necessary to avoid a serious inequity in the distribution of indirect costs, and with the approval of the cognizant agency for indirect costs.

New Investigator. A PD/PI who has not previously competed successfully as a PD/PI for a significant independent research award is considered a New Investigator. For example, a PD/PI who has previously received a competing NIH R01 research grant is no longer considered a New Investigator. However, a PD/PI who has received a Small Grant (R03) or an Exploratory/Developmental Research Grant Award (R21) retains his or her status as a New Investigator. A complete definition of a New Investigator along with a list of NIH grants that do not disqualify a PD/PI from being considered a New Investigator can be found at http://grants.nih.gov/grants/new_investigators/index.htm.See also the definition of Early Stage Investigator.

Non-Federal entity. Non-Federal entity means a state, local government, Indian tribe, institution of higher education (IHE), or nonprofit organization that carries out a Federal award as a recipient or subrecipient.

Nonprofit organization. Nonprofit organization means any corporation, trust, association, cooperative, or other organization, not including IHEs, that: (a) Is operated primarily for scientific, educational, service, charitable, or similar purposes in the public interest; (b) Is not organized primarily for profit; and (c) Uses net proceeds to maintain, improve, or expand the operations of the organization.

Notice of Award. The official, legally binding document, signed (or the electronic equivalent of signature) by a Grants Management Officer that:

(1) notifies the recipient of the award of a grant;

(2) contains or references all the terms and conditions of the grant and Federal funding limits and obligations; and,

(3) provides the documentary basis for recording the obligation of Federal funds in the NIH accounting system.

NRSA Individual Fellowship. Ruth L. Kirschstein National Research Service Award provided to individuals for research training in biomedical and behavioral research.

Office of Management and Budget (OMB). OMB means the Executive Office of the President, Office of Management and Budget.

OHRP. Office for Human Research Protections.

OLAW. Office of Laboratory Animal Welfare.

Other Significant Contributors. Individuals who have committed to contribute to the scientific development or execution of the project, but are not committing any specified measurable effort (i.e., person months) to the project. These individuals are typically presented at "zero percent" effort or "as needed." Individuals with measurable effort may not be listed as Other Significant Contributors. Consultants should be included if they meet this definition.

Pass-through entity (PTE). PTE means a non- Federal entity that provides a subaward to a subrecipient to carry out part of a Federal program.

Participant support costs. Participant support costs means direct costs for items such as stipends or subsistence allowances, travel allowances, and registration fees paid to or on behalf of participants or trainees (but not employees) in connection with conferences, or training projects. For the purposes of Kirschstein-NRSA programs, this term does not apply. NIH will continue to use the terms trainees, trainee-related expenses, and trainee travel in accordance with NRSA Regulations.

Payback. Requirement that the recipient of a NRSA postdoctoral fellowship engage in qualified research or teaching activities for a length of time equal to the period of NRSA support received. Only the first year of training incurs a payback obligation. In general, payback activity must involve at least 20 hours per week and be conducted over 12 consecutive months; special exceptions may be considered on a case-by-case basis.

Person Months. The metric for expressing the effort (amount of time) that PD/PIs, faculty and other senior/key personnel devote to a specific project. The effort is based on the type of appointment of the individual with the organization, e.g., calendar year (CY), academic year (AY), and/or summer term (SM); and the organization's definition of such. The effort is expressed as a percentage of the total institutional appointment.

Personally Identifiable Information (PII). PII means information that can be used to distinguish or trace an individual’s identity, either alone or when combined with other personal or identifying information that is linked or linkable to a specific individual. Some information that is considered to be PII is available in public sources such as telephone books, public Web sites, and university listings. This type of information is considered to be Public PII and includes, for example, first and last name, address, work telephone number, email address, home telephone number, and general educational credentials. The definition of PII is not anchored to any single category of information or technology. Rather, it requires a case-by-case assessment of the specific risk that an individual can be identified. Non-PII can become PII whenever additional information is made publicly available, in any medium and from any source, that, when combined with other available information, could be used to identify an individual.

Portfolio Company. For purposes of the SBIR/STTR programs, portfolio company means any company that is owned in whole or part by a venture capital operating company, hedge fund, or private equity firm.

Postdoctoral Scholar. An individual who has received a doctoral degree (or equivalent) and is engaged in a temporary and defined period of mentored advanced training to enhance the professional skills and research independence needed to pursue his or her chosen career path.

Principal Investigator, Program Director, or Project Director. The individual(s) designated by the applicant organization/recipient to have the appropriate level of authority and responsibility to direct the project or program to be supported by the award. The applicant organization may designate multiple individuals as program directors/principal investigators (PD/PIs) who share the authority and responsibility for leading and directing the project, intellectually and logistically. When multiple PD/PIs are named, each is responsible and accountable to official at the applicant organization/recipient, or as appropriate, to a collaborating organization for the proper conduct of the project, or program, or activity including the submission of all required reports. The presence of more than one PD/PI on an application or award diminishes neither the responsibility nor the accountability of any individual PD/PI.

Prior Approval. Written approval by an authorized HHS official, e.g., a designated IC GMO, evidencing prior consent before a recipient undertakes certain activities or incurs specific costs.

Private Equity Firm. For purposes of the SBIR/STTR programs, private equity firm has the meaning given the term "private equity fund" in section 13(h)(2) of the Bank Holding Company Act of 1956 (12 U.S.C. 1851(h)(2)). The private equity firm must have a place of business located in the United States and be created or organized in the United States, or under the law of the United States or of any State.

Program Income. Gross income earned by the applicant organization that is directly generated by a supported activity or earned as a result of the award. The *NIH Grants Policy Statement* contains a detailed explanation of program income, the ways in which it may be generated and accounted for, and the various options for its use and disposition.

Examples of program income include:

- Fees earned from services performed under the grant, such as those resulting from laboratory drug testing;
- Rental or usage fees, such as those earned from fees charged for use of computer equipment purchased with grant funds;
- Third party patient reimbursement for hospital or other medical services, such as insurance payments for patients when such reimbursement occurs because of the grant-supported activity;
- Funds generated by the sale of commodities, such as tissue cultures, cell lines, or research animals;
- Patent or copyright royalties (exempt from reporting requirements); and
- Registration fees generated from grant-supported conferences.

Protected Personally Identifiable Information (Protected PII). Protected PII means an individual's first name or first initial and last name in combination with any one or more of types of information, including, but not limited to, social security number, passport number, credit card numbers, clearances, bank numbers, biometrics, date and place of birth, mother's maiden name, criminal, medical and financial records, educational transcripts. This does not include PII that is required by law to be disclosed. (See also 200.79 Personally Identifiable Information (PII)).

Prototype. A model of something to be further developed and includes designs, protocols, questionnaires, software, and devices.

Recipient. The organizational entity or individual receiving a grant or cooperative agreement. See also definition for grantee.

Research or Research and Development (R/R&D). Any activity that is:

- A systematic, intensive study directed toward greater knowledge or understanding of the subject studied; or
- A systematic study directed specifically toward applying new knowledge to meet a recognized need; or
- A systematic application of knowledge toward the production of useful materials, devices, and systems or methods, including design, development, and improvement of prototypes and new processes to meet specific requirements.

Research Institution. A United States research organization that is:

- A nonprofit college or university; or
- A nonprofit research institution, including nonprofit medical and surgical hospitals. (A "nonprofit institution" is defined as an organization that is owned and operated exclusively for scientific or educational purposes, no part of the net earnings of which inures to the benefit of any private shareholder or individual.); or
- A contractor-operated, Federally funded research and development center, as identified by the National Science Foundation in accordance with the Government-wide Federal Acquisition Regulation issued in accordance with section 35(c)(1) of the Office of Federal Procurement Policy Act (or any successor legislation thereto).
- (Laboratories staffed by Federal employees do not meet the definition of "research institution" for purposes of the STTR program.)

SBIR/STTR Technical Data. All data generated during the performance of an SBIR/STTR award.

SBIR/STTR Technical Data Rights. The rights a small business concern obtains in data generated during the performance of any SBIR/STTR Phase I, Phase II, or Phase III award that an awardee delivers to the Government during or upon completion of a Federally-funded project, and to which the Government receives a license.

Scientific Rigor. The strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results. This includes full transparency in reporting experimental details so that others may reproduce and extend the findings.

Senior/Key Personnel. The PD/PI and other individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not salaries or compensation is requested under the grant.

> Typically these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level may be considered if their involvement meets the definition of senior/key personnel. Consultants and those with a postdoctoral role should also be included if they meet the definition of senior/key personnel. Senior/key personnel must devote measurable effort to the project whether or not salaries are requested--"zero percent" effort or "as needed" are not acceptable levels for those designated as senior/key personnel.

Socially and Economically Disadvantaged Individual. A member of any of the following groups: Black Americans; Hispanic Americans; Native Americans; Asian-Pacific Americans; Subcontinent Asian Americans; other groups designated from time to time by the Small Business Administration (SBA) to be socially disadvantaged; or any other individual found to be socially and economically disadvantaged by SBA pursuant to Section 8(a) of the Small Business Act, 15 U.S.C. 637(a). See 13 C.F.R. §§ 124.103 and 124.104.

Special Purpose Equipment. Special purpose equipment means equipment which is used only for research, medical, scientific, or other technical activities. Examples of special purpose equipment include microscopes, x-ray machines, surgical instruments, and spectrometers.

Sponsor/Co-Sponsor. One or more designated individual(s) responsible for providing the applicant with research training and career guidance throughout the grant award period.

Sponsoring Institution. Institution legally responsible for committing facilities for the Kirschstein-NRSA Individual Fellowship applicant and financially responsible for the use and disposition of fellowship funds.

State. State means any state of the United States, the District of Columbia, the Commonwealth of Puerto Rico, the Virgin Islands, Guam, American Samoa, the Commonwealth of the Northern Mariana Islands, and any agency or instrumentality thereof exclusive of local governments.

Stipend. A payment made to an individual under a fellowship or training grant in accordance with pre-established levels to provide for the individual's living expenses during the period of training. A stipend is not considered compensation for the services expected of an employee.

Subaward. Subaward means an award provided by a pass-through entity to a subrecipient for the subrecipient to carry out part of a Federal award received by the pass-through entity. It does not include payments to a contractor or payments to an individual that is a beneficiary of a Federal program. A subaward may be provided through any form of legal agreement, including an agreement that the pass-through entity considers a contract. The term includes consortium agreements.

Summary Statement. The official agency record of the evaluation and recommendations made by peer review groups. It contains the essentially unedited, verbatim critiques of two or more individuals assigned to review the grant application.

Supplies. Supplies means all tangible personal property other than those described in §200.33 Equipment. A computing device is a supply if the acquisition cost is less than the lesser of the capitalization level established by the non-Federal entity for financial statement purposes or $5,000, regardless of the length of its useful life.

Total Cost. The total cost of a Federal award is the sum of the allowable direct and allocable indirect costs less any applicable credits.

United States. The 50 states, territories and possessions of the U.S., Commonwealth of Puerto Rico, Trust Territory of the Pacific Islands, and District of Columbia.

Venture Capital Operating Company. For purposes of the SBIR/STTR programs, venture capital operating company means an entity described in § 121.103(b)(5)(i), (v), or (vi). The venture capital operating company must have a place of business located in the United States and be created or organized in the United States, or under the law of the United States or of any State.

4. General Information

4.1 Research Grant Activity Codes

The following tables summarize the major activity codes NIH uses to fund research grants. For more detailed information, visit the OER Web site http://grants.nih.gov/grants/funding/funding_program.htm.

NIH continues to transition applications from the PHS398 to the SF424 (R&R) and electronic submission through Grants.gov by grant activity code. Some of the activity codes described in the chart below have already transitioned; others will transition in the near future. Applicants should refer to the Timeline to determine when a particular activity code has transitioned to the new form and electronic submission: http://grants.nih.gov/grants/ElectronicReceipt/files/timeline_NIH_transitions.pdf.

For more information on NIH's transition plans, see the Web site for Electronic Submission of Grant Applications: http://grants.nih.gov/grants/ElectronicReceipt/.

Research Grants

TYPE (ACTIVITY CODE)	DESCRIPTION
Basic Research Grant (R01) http://grants.nih.gov/grants/funding/r01.htm	Basic Research Grants are awarded to eligible institutions on behalf of a principal investigator to support a discrete project related to the investigator's area of interest and competence. These grants make up the largest category of NIH funding.
Small Research Grant (R03) http://grants.nih.gov/grants/funding/r03.htm	Small Research Grants support small research projects that can be carried out in a short period of time with limited resources for projects such as pilot or feasibility studies; secondary analysis of existing data; small, self-contained research projects; development of research methodology and/or development of new research technology. Not all awarding components accept investigator-initiated R03 applications. Applicants interested in the small research grant program of PHS-awarding components other than NIH should contact an official of the appropriate PHS-awarding component (See Part I, 1.4, of the SF424 (R&R) SBIR/STTR Application Guide.)
Academic Research Enhancement Award (AREA) (R15) http://grants.nih.gov/grants/funding/area.htm	Academic Research Enhancement Awards provide support to scientists at eligible domestic institutions for small-scale health-related research projects, such as pilot research projects and feasibility studies; development, testing, and refinement of research techniques; and similar discrete research projects that demonstrate research capability. This award is directed toward those smaller public and private colleges and universities that provide undergraduate training for a significant number of the U.S. research scientists.

TYPE (ACTIVITY CODE)	DESCRIPTION
Exploratory/Developmental Research Grant (R21/R33) http://grants.nih.gov/grants/funding/r21.htm	Exploratory/Developmental Research Grants seek to broaden the base of inquiry in fundamental biomedical research by encouraging applications for research projects that involve an especially high degree of innovation and novelty. NIH provides pilot-scale support for potentially ground-breaking ideas, methods, and systems that meet the following criteria: they lack sufficient preliminary data for feasibility to be established, their successful demonstration would have a major impact on biomedical research, and they fall within the areas supported by the awarding I/C. Not all awarding components accept R21/R33 applications.
Small Business Innovation Research Grant (SBIR: R43/R44) **Small Business Technology Transfer Grant (STTR: R41/R42)** http://grants.nih.gov/grants/funding/sbir.htm	SBIR and STTR grants are made to eligible domestic for-profit small business concerns conducting innovative research that has the potential for commercialization. SBIR/STTR awards are intended to stimulate technological innovation, use small business to meet Federal research and development needs, increase private sector commercialization of innovations derived from Federal research and development, and foster and encourage participation by minority and disadvantaged persons in technological innovation.
Program Project Grant (P01)	Program Project Grants are more complex in scope and budget than the individual basic research (R01) grant. While R01s are awarded to support the work of one principal investigator who, with supporting staff, is addressing a scientific problem, program project grants are available to a group of several investigators with differing areas of expertise who wish to collaborate in research by pooling their talents and resources. Program project grants represent synergistic research programs that are designed to achieve results not attainable by investigators working independently. Not all awarding components accept P01 applications.
Research Center Grant (P50/P60)	Research Center Grants serve varying scientific and IC-specific purposes, but they have elements in common. The grants are multidisciplinary in scope and may focus more on an area or discipline of science than on a specific theme or goal. Independent investigators direct the projects and cores. Center grants offer a greater opportunity for scientific interactions and overall progress than with individually-funded projects. Not all awarding components accept P50/P60 applications.

TYPE (ACTIVITY CODE)	DESCRIPTION
Scientific Meeting Support (R13) http://grants.nih.gov/grants/funding/r13/index.htm	Most NIH ICs provide support for scientific meetings, conferences, and workshops that are relevant to its scientific mission. Any U.S. institution or organization, including an established scientific or professional society, is eligible to apply. For more information and guidelines, see http://grants.nih.gov/grants/guide/pa-files/PAR-03-176.html. Applicants must obtain IC approval prior to submission.

Training, Fellowships and Career Development Programs

TYPE (ACTIVITY CODE)	DESCRIPTION
Institutional Research Training Including Ruth L. Kirschstein National Research Service Awards (T32/T34/T35) http://grants.nih.gov/training/nrsa.htm	These awards are made to domestic institutions that have the facilities and faculty to provide for research training programs in scientific specialties. Grant funds may be used for personnel, equipment, supplies, trainee stipends (both pre- and postdoctoral), and related costs.
Individual Ruth L. Kirschstein National Research Service Award Fellowships) (NRSA: F30/F31/F32/F33) https://researchtraining.nih.gov/programs/fellowships	These fellowships are awarded to qualified individuals at the predoctoral, postdoctoral, or senior investigator level to pursue full-time research training in designated biomedical or behavioral science areas.
Career Development Award (K Award) http://grants.nih.gov/training/careerdevelopmentawards.htm	Among NIH components, several types of career development awards are available to research and academic institutions on behalf of scientists who require additional independent or mentored experience in a productive scientific environment in order to further develop their careers in independent biomedical or behavioral research.

Applications Available from Other Offices

APPLICATION	CONTACT
Nonresearch Training Grant Application (PHS 6025)	Health Resources and Services Administration (HRSA) (301) 443-6960
Health Services Project Application (5161-1)	Substance Abuse and Mental Health Services Administration (SAMHSA) (301) 436-8451

4.2 Mail Addressed to the National Institutes of Health

All United States Postal Service (USPS) mail addressed to the National Institutes of Health must use the unique NIH zip code 20892. All USPS mail addressed to the National Library of Medicine should use the unique NLM zip code of 20894. All mail using 20892 and 20894 zip codes will be cleared through the NIH North Stonestreet Mail Facility. This will ensure that special procedures and precautions will be used to screen the mail before it is delivered to the various NIH offices on and off campus. This is an important measure to provide for the safety of all individuals who must handle mail.

This procedure does not apply to commercial courier deliveries (i.e. FEDEX, UPS, DHL, etc.) of grant applications addressed to the Center for Scientific Review. The zip code for these deliveries is 20817. All applications and other deliveries to the Center for Scientific Review must either come via courier delivery or the USPS.

NIH WILL NOT ACCEPT APPLICATIONS **DELIVERED BY INDIVIDUALS** TO THE CENTER FOR SCIENTIFIC REVIEW. This restriction does not apply to USPS or courier delivery personnel.

Mail addressed to NIEHS in North Carolina should continue to show zip code 27709.

4.3 Government Use of Information Under Privacy Act

The NIH maintains application and grant records as part of a system of records as defined by the Privacy Act: NIH 09-25-0036, *Extramural Awards and Chartered Advisory Committees (IMPAC 2), Contract Information (DCIS), and Cooperative Agreement Information*,
HHS/NIH: http://oma.od.nih.gov/public/MS/privacy/pafiles/0036.htm.

4.4 Information Available to the Program Director(s)/Principal Investigator(s)

Under the provisions of the Privacy Act, PD/PIs may request copies of records pertaining to their grant applications from the PHS component responsible for funding decisions. PD/PIs are given the opportunity under established procedures to request that the records be amended if they believe they are inaccurate, untimely, incomplete, or irrelevant. If the PHS concurs, the records will be amended.

4.5 Information Available to the General Public

PHS makes information about grant awards available to the public, including the title of the project, the grantee institution, the PD/PI, and the amount of the award. The description on Form Page 2 of a funded research grant application is sent to the National Technical Information Service (NTIS), U.S. Department of Commerce, where the information is available to the public and used for the dissemination of scientific information and for scientific classification and program analysis purposes. In addition, NIH routinely places information about awarded grants, including project title, name of the PD/PI, and project description (abstract) in the RePORT system.

Freedom of Information Act Requirements

The Freedom of Information Act and implementing HHS regulations (45 CFR part 5) require the release of certain information about grants upon request, regardless of the intended use of the information. Generally available for release upon request are: all funded grant applications and progress reports including their derivative funded non-competing supplemental grant progress reports; pending and funded non-competing continuation progress reports; progress reports of grantees; and final reports of any review or evaluation of grantee performance conducted or caused to be conducted by the HHS. Generally **not** available for release to the public are: competing grant progress reports (new, resubmission, renewal, and revisions) for which awards have **not** been made; evaluative portions of site visit reports; and summary statements of findings and recommendations of review groups. Trade secrets and commercial, financial, or otherwise proprietary information may be withheld from disclosure. Information, which, if disclosed, would be a clearly unwarranted invasion of personal privacy, may also be withheld from disclosure. Although the grantee institution and the principal investigator will be consulted about any such release, the PHS will make the final determination. Any indication by the applicant that the application contains proprietary or privileged information does not automatically shield the information from release in response to a Freedom of Information Act (FOIA) request should the application result in an award (see 45 CFR Part 5). If an applicant fails to identify proprietary information at the time of submission as instructed in the application guide, a significant substantive justification will be required to withhold the information if requested under FOIA. If a requested document contains both

disclosable and nondisclosable information, the nondisclosable information will be deleted and the balance of the document will be released.

4.6 Access to Research Data

As required by regulation 45 CFR 75.322, grantees that are institutions of higher education, hospitals, or non-profit organizations must release "research data" first produced in a project supported in whole or in part with Federal funds if they are cited publicly and officially by an HHS awarding agency in support of an action that has the force and effect of law (i.e., regulations and administrative orders). The term "research data" is defined as the recorded factual material commonly accepted in the scientific community as necessary to validate research findings. It does not include preliminary analyses; drafts of scientific papers; plans for future research; peer reviews; communications with colleagues; physical objects (e.g., laboratory samples, audio or video tapes); trade secrets; commercial information; materials necessary to be held confidential by a researcher until publication in a peer-reviewed journal; information that is protected under the law (e.g., intellectual property); personnel and medical files and similar files, the disclosure of which would constitute an unwarranted invasion of personal privacy; or information that could be used to identify a particular person in a research study.

This requirement to release research data does not apply to commercial organizations or to research data produced by state or local governments. However, if a state or local governmental grantee contracts with an IHE, hospital or non-profit organization, and the contract results in covered research data, those data are subject to these disclosure requirements. See http://grants.nih.gov/grants/policy/data_sharing/index.htm.

5. SBIR/STTR Award Guidelines, Reporting Requirements, and Other Considerations

5.1. Awards and Cost Principles

Most NIH grant awards provide for cost reimbursement (as contrasted with fixed-price arrangements) and are subject to government-wide or HHS-wide cost principles. The cost principles establish standards for the allowability of costs, provide detailed guidance on the cost accounting treatment of costs as direct or F&A costs, and set forth allowability principles for selected items of cost. Applicability of a particular set of cost principles depends on the type of organization making the expenditure. For example, a for-profit organization collaborating with a university grantee would be subject to the cost principles for commercial organizations, while the university would be subject to the cost principles for IHEs.

The cost principles are set forth in the following documents 45 CFR part 75, Subpart E, and the following documents. The cost principles apply to all NIH SBIR/STTR grants, award mechanisms, and special programs and authorities, including modular awards and awards under SNAP.

- 45 CFR part 75, Appendix IX – Cost Principles for Hospitals
- 48 CFR Subpart 31.2 (Federal Acquisition Regulation) – Cost Principles for Commercial Organizations

Grantees are able to use their own previously developed accounting systems, policies, and procedures to implement the cost principle requirements as long as the standards prescribed in CFR 75.302 for financial management systems are met.

5.2. Terms and Conditions of Award

Pre-award Costs. A potential grantee may, *at its own risk* and without NIH prior approval, incur obligations and expenditures to cover costs up to 90 days prior to the effective date of a new or competing continuation award if such costs:

- Are necessary to conduct the project, and
- Would be allowable under the grant, if awarded, without NIH prior approval.

Upon acceptance of a grant award, the grantee must comply with the terms and conditions contained or referenced in the Notice of Award document. These terms and conditions, constituting legal requirements imposed on an awardee by statute, regulations, administrative policy, or the award document itself, are either "standard" or "special" as follows:

Standard Terms and Conditions. Those that are required by policy to be incorporated by reference in Notices of Grant Award through citations of specific documents that contain requirements applicable to the grant.

Special Terms and Conditions. Those that are judged necessary to attain the objectives for which the grant is being awarded, facilitate post-award administration, conserve grant funds, or otherwise protect the interests of the Federal Government. They are stated in full on the Notice of Award.

NIH Standard Terms of Award. Under NIH Standard Terms of Award of the NIH Grants Policy, the grantee organization may elect to extend the project period for up to 12 months without additional funds. At least 10 days prior to the original project end date, the grantee must *notify* the awarding agency Grants Management Official (GMO) in writing (e-mail, letter, or eRA Commons) of the extension. The notification must be signed by the authorizing business official and must include the new project end date. Extensions beyond the initial notification must be *requested* by the grantee organization and *approved* by the awarding GMO.

Grant awards must be administered in accordance with the current NIH Grants Policy Statement , including the Public Policy Requirements outlined in Chapter 4 and requirements specific to For-Profit Institutions outlined in Chapter 18.

Life Cycle Certification. All SBIR and STTR awardees must complete a life cycle certification at all times set forth in the Notice of Award. Awardees are not required to submit this certification directly to the NIH but must complete and maintain it on file in accordance with the records retention policy in NIH Grants Policy Statement Section 8.4.2. A certification is required at the following times:

- For SBIR & STTR Phase I Awardees: At the time of receiving final payment or disbursement from the Payment Management System
- For SBIR & STTR Phase II Awardees: prior to receiving more than 50% of the total award amount and prior to final payment or disbursement from the Payment Management System.

In addition, SBIR/STTR awardees indicate compliance with these certification requirements by drawing or requesting funds from the Payment Management System. If the grantee cannot complete this certification or cannot ensure compliance with the certification process, it should notify the GMO immediately. If resolution cannot be reached, the GMO will void or terminate the grant, as appropriate. The certification forms are available in fillable format at: http://grants.nih.gov/grants/forms.htm#sbir. For additional information on this requirement, SBIR grantees should refer to NIH Grants Policy Statement Section 18.5.5.4; STTR grantees should refer to section 18.5.5.5.

5.3 Payment Schedule

Payments for SBIR/STTR grants awarded by NIH are made through the Division of Payment Management http://www.dpm.psc.gov/. Once an SBIR/STTR grant is awarded, the grantee will receive information and forms from the Payment Management System of the HHS regarding requests for cash, manners of payment, and associated reporting requirements. Payment may be made on a cost-reimbursement or advance basis.

For further information on payment and interest earned on advances of grant funds, see Chapter 6 of the current NIH Grants Policy Statement.

The cost principles for for-profit institutions are set forth in 48 CFR Subpart 31.2 (Federal Acquisition Regulation) – Cost Principles for Commercial Organizations and are incorporated by reference in 45 CFR 75.401. SBIR/STTR grantees are able to use their own previously developed accounting systems, policies, and

procedures to implement the cost principle requirements as long as the standards prescribed in 45 CFR 75.302 for financial management systems are met. See Chapter 6, Payment, of the NIH Grants Policy Statement for further information.

5.4 Reports

Grantees are responsible for managing the day-to-day operations of grant-supported activities using their established controls and policies, as long as they are consistent with NIH requirements. However, to fulfill their role in regard to the stewardship of Federal funds, NIH awarding ICs monitor their grants to identify potential problems and areas where technical assistance might be necessary. This active monitoring is accomplished through review of reports and correspondence from the grantee, audit reports, site visits, and other information available to NIH. The names and telephone numbers of the individuals responsible for monitoring the programmatic and business management aspects of a project or activity will be provided to the grantee at the time of award.

Monitoring of a project or activity will continue for as long as NIH retains a financial interest in the project or activity as a result of property accountability, audit, and other requirements that may continue for a period of time after the grant is administratively closed out and NIH is no longer providing active grant support.

NIH requires that grantees periodically submit financial and progress reports. Other required reports may include annual invention utilization reports, lobbying disclosures, conflict of interest reports, audit reports, reports to the appropriate payment points (in accordance with instructions received from the payment office), and specialized programmatic reports.

SBIR/STTR grantees generally must meet the following reporting requirements:

- Cash Transaction and Financial Expenditure Reports
- Annual Progress Report
- Final Progress Report
- Final Invention Statement and Certification (HHS 568)
- Annual Invention Utilization Reports
- Phase II Data Collection Requirement for Government SBIR.gov database.

* Note: Progress reports usually are required annually as part of the non-competing continuation request or competing renewal application. However, NIH may require these reports more frequently. The information to be included in the progress report as part of a non-competing continuation request is specified in the PHS-2590 progress report instructions or the Research Performance Progress Report (RPPR), which also include the alternate instructions for awards under Streamlined non-competing process (SNAP) (see "Administrative Requirements—Non-Competing Continuation Awards" of the *NIH Grants Policy Statement*).

Non-competing grant progress reports must be submitted directly to the awarding office. Grantees should routinely query and review the list of pending grant progress reports and due dates available at the NIH website.

Grantees are allowed a specified period of time in which to submit required interim and final financial and progress reports (see CFR 75.341, 75.342, and 75.381). Failure to submit complete, accurate, and timely reports may indicate the need for closer monitoring by NIH or may result in possible award delays or enforcement actions, and may affect future funding to the organization or awards with the same principal investigator.

See Chapter 8.4 of the current NIH Grants Policy Statement for further information on monitoring and grant reporting requirements. Additionally, see Chapter 8.6 for an explanation of grant closeout reports and procedures.

Reporting Requirements Specific to SBIR/STTR Grants

Phase I Final Progress Report: If a Phase I awardee does not intend to submit a Phase II application within four months of the Phase I project period end date, then an original and one copy of the Phase I Final Progress Report must be submitted to the Grants Management Office of the Awarding Component *within 90 days* of the expiration of the Phase I grant period. Otherwise, the Phase I Final Report is a required part of the Phase II application.

There is no "form page" for a Final Report; however, instructions for the Final Progress Report are found at: http://grants.nih.gov/grants/forms.htm#closeout. See in particular, Part C. Instructions for SBIR/STTR Phase II Final Progress.

Phase II Data Collection Requirement for Government SBIR Reporting Database: The SBA maintains a Database System on SBIR.gov to track and report on statistics regarding the SBIR and the STTR programs.

Each small business concern applying for a Phase II award is required to update the appropriate information in the reporting database on SBIR.gov for any of its prior Phase II awards.

In meeting this requirement, the small business concern may apportion sales or additional investment information relating to more than one Phase II award among those awards, if it notes the apportionment for each award. Each Phase II awardee is required to update the appropriate information in the SBIR database on that award upon completion of the last deliverable (e.g., Final Report, Financial Status Report, Invention Report) under the funding agreement. In addition, the awardee is requested to voluntarily update the appropriate information on that award in the SBIR database annually thereafter for a minimum period of 5 years.

Questions about this requirement may be submitted to SBA directly through the Contact Us/Send Feedback link on SBIR.gov. To register on and use the database system, visit http://sbir.gov. Online help is available. SBA will minimize the data reporting requirements of small business concerns, make updating available electronically, and provide standardized procedures.

Project commercialization and sales data can only be viewed by Congress, General Accounting Office (GAO), agencies participating in the SBIR/STTR programs, Office of Management and Budget (OMB), Office of Science and Technology Policy (OSTP), Office of Federal Procurement Policy (OFPP), and other authorized persons (for example, authorized contractors) who are subject to a use and nondisclosure agreement with the Federal Government covering the use of the database. Pursuant to 15 U.S.C. 638(k)(4), information provided to the SBIR.gov database is privileged and confidential and not subject to disclosure pursuant to 5 U.S.C. 552 (Government Organization and Employees); nor must it be considered to be publication for purposes of 35 U.S.C. 102 (a) or (b).

Examples of the data to be entered by applicants into SBIR.gov include revenue from the sale of new products or services resulting from the research conducted under each Phase II award or additional investment from any source, other than Phase I or Phase II awards, to further the research and development conducted under each Phase II award.

5.5 Innovations, Inventions and Patents

According to NIH Grants Policy and Federal law, NIH recipient organizations must promptly report all inventions that are either conceived or first actually reduced to practice using NIH grant funds.

NIH strongly supports electronic reporting through an Internet-based system, Interagency Edison (https://s-edison.info.nih.gov/iEdison/). To meet the objectives of the Federal Financial Assistance Management Improvement Act of 1999 (P.L. 106-107), grantees should make all reasonable efforts to submit invention reports using iEdison. The system supports confidential transmission of required information and provides a utility for generating reports and reminders of pending reporting deadlines. Further information about the system, including instructions for creating an account needed to submit reports electronically, are on the iEdison site (http://www.iedison.gov).

Inquiries or correspondence should be directed to *Extramural Inventions and Technology Resources Branch of the Office of Policy for Extramural Research Administration, OER, NIH, 6705 Rockledge Dr., MSC 7980, Bethesda, MD 20892-7980, (301) 435-1986*. Information from these reports is retained by the NIH as confidential and submission does not constitute any public disclosure. Failure to report as described at 37 CFR Section 401.14 is a violation of 35 U.S.C. 202 and may result in loss of the rights of the recipient organization.

See Section 8.4.1.6, Invention Reporting, of the current *NIH Grants Policy Statement* for further explanation.

Limited Rights Information and Data

Proprietary Information

Applicants are discouraged from submitting information considered proprietary unless it is deemed essential for proper evaluation of the application. However, when the application contains information that constitutes trade secrets, information that is commercial or financial, or information that is confidential or privileged, make sure you have checked the "Yes" box of question #3 in the "Other Project Information" Form.

When information in the application constitutes trade secrets or information that is commercial or financial, or information that is confidential or privileged, it is furnished to the Government in confidence with the understanding that the information shall be used or disclosed only for evaluation of this application. If a grant is awarded because of or in connection with the submission of this application, the Government shall have the right to use or disclose the information to the extent authorized by law. This restriction does not limit the Government's right to use the information if it is obtained without restriction from another source.

Information contained in unfunded grant applications will remain the property of the applicant. The Government may, however, retain copies of all applications submitted. Public release of information in any application submitted will be subject to existing statutory and regulatory requirements.

Title to Equipment and Supplies

Title to equipment and supplies acquired by a for-profit organization as a grantee or subcontractor under a grant awarded by the HHS agencies participating in this solicitation, shall vest, upon acquisition, in the grantee or subcontractor, respectively. Final disposition of equipment acquired with Federal funds by for-profit grantees is covered under CFR 75.320. See Section 18.4.1, Equipment Accountability, of the current *NIH Grants Policy Statement* for further information.

Rights in Data Developed Under SBIR/STTR Funding Agreement

To preserve the SBIR data rights of the awardee, the legend (or statements) used in the SBIR Data Rights clause included in the SBIR award must be affixed to any submissions of technical data developed under that SBIR award. If no Data Rights clause is included in the SBIR award, the following legend, at a minimum, should be affixed to any data submissions under that award:

"These SBIR data are furnished with SBIR rights under Funding Agreement No. _____ (and subcontract No. _____ if appropriate), Awardee Name _____, Address, Expiration Period of SBIR Data Rights _____. The Government may not use, modify, reproduce, release, perform, display, or disclose technical data or computer software marked with this legend for (choose four (4) or five (5) years). After expiration of the (4- or 5-year period), the Government has a royalty-free license to use, and to authorize others to use on its behalf, these data for Government purposes, and is relieved of all disclosure prohibitions and assumes no liability for unauthorized use of these data by third parties, except that any such data that is also protected and referenced under a subsequent SBIR award shall remain protected through the protection period of that subsequent SBIR award. Reproductions of these data or software must include this legend."

Rights to data, including software developed under the terms of any funding agreement resulting from a grant application submitted in response to this solicitation, shall remain with the grantee, except that the Government shall have the limited right to use such data for internal Government purposes and shall not release such data outside the Government without permission of the grantee for a period of four years from completion of the

project from which the data were generated. See Section 18.5.5.2, Intellectual Property, of the current *NIH Grants Policy Statement* for further explanation.

Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single budget period are expected to include a plan for data sharing or state why data sharing is not possible. See Section 18.5.5.3, Data Sharing, of the current *NIH Grants Policy Statement* for further information.

Copyrights

The grantee may normally copyright and publish (consistent with appropriate national security considerations, if any) material developed with PHS support. The awarding component receives a royalty-free license for the Federal Government. Each publication, press release, or other document about research supported by an NIH grant must include:

1) An acknowledgment of NIH grant support such as:

> "Research reported in this [publication, release] was supported by [name of the Institute, Center, or other funding component] of the National Institutes of Health under grant number [specific NIH grant number in this format: R01GM012345]."

2) A disclaimer that says:

> "The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health" and requires that each publication contain an acknowledgment of agency support and disclaimer statement, as appropriate. An acknowledgment shall be to the effect that *"This publication was made possible by grant number _____ from (NIH/CDC/FDA awarding component)"* OR *"The project described was supported by grant number _____ from (NIH/CDC/FDA awarding component). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the (NIH/CDC/FDA awarding component).*

See Section 8.2.1, Rights in Data (Publication and Copyrighting), of the current *NIH Grants Policy Statement* for further information.

Inventions

Refer to http://www.iedison.gov *and Section 8.2.4, Inventions and Patents, of the current NIH Grants Policy Statement for more detailed information.*

Any invention first conceived or reduced to practice with award funds must be reported to the NIH. *The inventor must report the discovery to the grantee organization promptly*. Within two months of the inventor's initial report to the grantee organization, the organization must report the invention to the NIH's Extramural Invention Reporting and Technology Resources Branch of the Office of Policy for Extramural Research (see address in "Patents" section below). This should be done prior to any publication or presentation of the invention at an open meeting, since failure to report at the appropriate time is a violation of 35 U.S.C. 202, and may result in loss of the rights of the small business concern, inventor, and Federal Government in the invention. All foreign patent rights are immediately lost upon publication or other public disclosure unless a United States patent application is already on file. In addition, statutes preclude obtaining valid United States patent protection after one year from the date of a publication that discloses the invention.

NIH strongly supports electronic reporting through an Internet-based system, Interagency Edison (https://s-edison.info.nih.gov/iEdison/). Use of the iEdison system satisfies all mandated invention reporting requirements and access to the system is through a secure interactive Web site (http://www.iedison.gov) designed to ensure that all information submitted is confidential.

In addition to fulfilling reporting requirements, iEdison notifies the user of future time-sensitive deadlines with enough lead-time to avoid the possibility of loss of patent rights due to administrative oversight. IEdison can accommodate the invention reporting needs of all organizations. For additional information about this invention

reporting and tracking system, *visit the iEdison home page cited above or contact Edison via e-mail at* edison@od.nih.gov.

Patents

Small business concerns normally retain the principal worldwide patent rights to any invention developed with Government support. Under existing regulations, 37 CFR 401, the Government receives a royalty-free license for Federal Government use, reserves the right to require the patent-holder to license others in certain circumstances, and requires that anyone exclusively licensed to sell the invention in the United States must normally manufacture it substantially in the United States. The applicant small business concern is *strongly encouraged to obtain information about additional requirements imposed by 37 CFR 401 from local counsel or from*:

Extramural Inventions and Technology Resources Branch
Office of Policy for Extramural Research
National Institutes of Health
6705 Rockledge Drive, MSC 7980
Bethesda, MD 20892-7750
Phone: (301) 435-1986; Fax: (301) 480-0272
E-mail: edison@od.nih.gov.

To the extent authorized by 35 U.S.C. 205, the Government will not make public any information disclosing a Government-supported invention for a four-year period from the date of disclosure (that may be extended by subsequent SBIR/STTR funding agreements) to allow the grantee a reasonable time to file a patent application, nor will the Government release any information that is part of that patent application.

Research Tools/Unique Research Resources

It is the policy of the NIH to make available to the public the results and accomplishments of the activities it funds. Restricted availability of unique research resources, upon which further studies are dependent, can impede the advancement of research and delivery of medical care. Notices in the *NIH Guide for Grants and Contracts* (Contracts (Volume 25, Number 23, July 12, 1996), http://grants.nih.gov/grants/guide/notice-files/not96-184.html) and "Availability of Research" in chapter 8 of the *NIH Grants Policy Statement* fully explain the policy regarding the distribution of research resources developed with NIH funds.

The NIH encourages the commercialization of research products and allows grantee organizations to make materials available to others for commercial purposes with appropriate restrictions and licensing terms. Where the product of research developed with Federal funding is a patentable but unpatented research product, the terms of a license must be no more restrictive than they would have been if the product had been patented.

See Section 8.2.3, Sharing Research Resources, of the current *NIH Grants Policy Statement* for further explanation.

5.6 Joint Ventures and Limited Partnerships

Joint ventures and limited partnerships are eligible provided the entity created qualifies as a small business concern in accordance with the definition in Section III. Size determination of a joint venture entity requires that the combined total number of employees from all affiliates not exceed 500. Other criteria under the definition of a small business concern must also be met.

5.7 American-Made Equipment and Products

When purchasing equipment or a product under the SBIR/STTR award, the small business concern should purchase only American-made items whenever possible.

5.8 Profit or Fee

A reasonable profit/fee is available to small business concerns receiving awards under the SBIR/STTR program; *however, this profit/fee must be included in your budget request at the time of application*. The fee is not a "cost" item and may be used by the small business concern for any purpose, including additional effort under the SBIR/STTR award. The fee is intended to be a reasonable profit factor available to for-profit organizations, consistent with normal profit margins provided to profit-making firms for research and development work. However, the amount of the fee approved by the agencies participating in this solicitation normally will not exceed 7% of total costs (direct and indirect) for each phase (I and II) of the project.

Example:
$70,000 direct costs (includes all third party costs) + $28,000 F&A costs (40% * 70,000) = $98,000.
Maximum allowable fee = 7% * $98,000 = $6,860 fee. Total Award = $104,860.

The profit/fee applies solely to the small business concern (grantee organization) receiving the SBIR/STTR award and not to any other participant in the project. However, the grantee may pay a profit/fee to a contractor providing routine goods or services in accordance with normal commercial practice.

5.9 Audit Requirements of For-Profit Organizations

A for-profit organization is required to have a non-Federal audit if, during its fiscal year, it expended a total of $750,000 or more in Federal awards. 45 CFR 75 addresses audit requirements for commercial organizations and provides two options (1) a financial-related audit (as defined in, and in accordance with, the Government Auditing Standards (commonly known as the "Yellow Book"), GPO stock 020-000-00-265-4, of a particular award in accordance with Government Auditing Standards, in those cases where the recipient receives awards under only one HHS program, or (2) an audit that meets the requirements of CFR 75, Subpart F. See Chapter 18.4.5 of the *NIH Grants Policy Statement* for further information.

5.10 Time and Effort Reporting for Commercial Organizations

Policy

Commercial (for-profit) organizations must document salaries and wages charged to contracts and grants by maintaining a labor distribution system for all employees regardless of function. The labor distribution system must account for total hours and charge direct and indirect labor to the appropriate cost objectives to accurately identify labor costs:

- Charged to direct projects.
- Charged to indirect activities.
- Included in the base to which indirect costs are allocated.

Internal Controls

Timekeeping procedures and controls on labor charges are of utmost concern. Unlike other costs, labor is not supported by external documentation or physical evidence, which provides independent checks and balances. It is critical that managers indoctrinate individual employees on their independent responsibility for accurately recording their time. Internal controls over labor charging should meet the following criteria:

- Responsibility for timekeeping and payroll accounting should be separated.
- Procedures must be clear and reasonable so there is no confusion regarding the rationale for the controls or misunderstanding as to what is and is not permissible.
- Maintenance of controls must be verified continually, and violations must be acted upon promptly and effectively to serve as a deterrent to prospective violations.

- Individual employees must be constantly made aware of controls that act as an effective deterrent against violations. This awareness can be accomplished by emphasizing the importance of accurate time and effort reporting in orientation sessions, periodic meetings, and the posting of messages as reminders.
- Changes on timesheets to the number of hours recorded or the cost center identified should be made by the employee and must be initialed by the employee.
- Company policy must state that the nature of the work performed determines the proper distribution of time, not the availability of funding, type of contract/grant, or other factors.
- Company policy should emphasize that complete and accurate time and effort reporting is an important part of an employee's job. Careless or improper reporting may lead to disciplinary actions under company policies as well as applicable Federal statutes.

Time and Effort Documentation Requirements and Responsibilities

Detailed instructions for time documentation should be established in written company procedures. A manual system would require handwritten pen and ink entries on a paper timesheet reflecting all the days in the pay period. An automated timekeeping system typically would use remote data entry for recording labor charging data and sending it directly to a central computer for processing. Supporting documentation for an automated system would normally consist of computer printouts showing data that appear on source documents, i.e., timesheets in a manual system.

Employee Responsibilities

Whether a manual or automated time and effort reporting system is in place, the employee is personally responsible for:

- After the fact recording of hours (or fractions thereof) on a daily basis.
- Recording all hours worked and all hours absent. All hours should be recorded whether or not they are paid.
- Recording of hours on the timesheet in ink (manual system only).
- Recording the correct distribution of hours by project or indirect category. The nature of the work performed determines the proper distribution of time, not the availability of funding, type of contract/grant, or other factors.
- To ensure accuracy, a listing of project numbers/indirect categories and their descriptions should be provided in writing to each employee.
- Any changes/corrections to timesheets should be made by the employee and must show what was initially recorded, i.e., no erasures or “white out” of entries.
- The employee also must initial any change(s).
- At the end of each pay period, the employee must sign the timesheet or electronically certify the labor distribution in an automated system.

Supervisor Responsibilities

- An authorized company official (e.g., supervisor) must cosign timesheets or electronically certify individual time and effort reporting at the end of each pay period.

The supervisor is prohibited from completing an employee's timesheet or entering hours in an automated system unless the employee is absent for an extended period of time on some form of authorized leave.

The SBIR Program is not a substitute for existing unsolicited proposal mechanisms. Unsolicited proposals must not be accepted under the SBIR or STTR Program in either Phase I or Phase II. All HHS SBIR and STTR grant applications to the National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), and the Food and Drug Administration (FDA) must be submitted electronically through the Federalwide portal Grants.gov (http://www.grants.gov) using the SF424 Research and Related (R&R) forms and the SF424 (R&R) SBIR/STTR Application Guide. All SBIR and STTR applications must be in response to a funding opportunity announcement (FOA) for the electronic submission of applications as announced in http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-067.html**.**

If an award is made pursuant to a proposal submitted under this SBIR/STTR Program solicitation, a representative of the contractor or grantee or party to a cooperative agreement will be required to certify that the concern has or is currently being, paid for essentially equivalent work by any Federal agency.