U.S. Department of Health and Human Services

Public Health Service

Grant Application (PHS 398)

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PART I

Instructions for Preparing and Submitting an Application

1. Foreword

The PHS 398 instructions contain information for preparing grant applications to the National Institutes of Health (NIH) and other Public Health Service agencies.

Applicants to PHS agencies other than NIH should contact the agency using the PHS Agency Contacts Table in 1.4 below because some awarding components have application requirements that differ from those for NIH.

NIH continues to transition grant activity codes from the PHS 398 to the SF424 (R&R) and electronic submission through Grants.gov. This PHS 398 is required for all grant activity codes that have not transitioned to the SF424 (R&R), including Resubmission, Renewal, Revision, changes of grantee institution, and cooperative agreement applications. Once an activity code has transitioned to electronic submission the applicant must apply through Grants.gov using the SF424 (R&R) and electronic PHS 398 components that are provided as part of the electronic application forms.

For more information on NIH's transition plans, including a timeline for the transition of various activity codes, see the website for Electronic Submission of Grant Applications: http://era.nih.gov/ElectronicReceipt/.

Bookmark this website (**http://grants.nih.gov/grants/funding/phs398/phs398.html**) for easy electronic access to this document.

Policy Changes

These instructions incorporate numerous clarifications, updates and policy announcements that have appeared in the NIH Guide for Grants and Contracts since the 11/2007 revision of the PHS 398 application. Since the Guide also publishes multiple funding opportunity announcements, the Office of Extramural Research posts Policy Notices, clarifications and other updates on this webpage: NIH Policy Notices. Applicants are expected to be aware of any relevant Notices that appear in the Guide.

Substantive changes to instructions and form pages fall into the following categories and are highlighted as follows:

Enhancing Peer Review Initiative (http://enhancing-peer-review.nih.gov/index.html)

- The Research Plan is restructured and aligned with peer review criteria.
- Shorter page limits are adopted for Rs (except R25), with other activity codes scaled accordingly.
- The Biographical Sketch now requires a Personal Statement, and encourages applicants to limit the number of publications to 15.
- Instructions for describing Resources are modified to address the scientific environment and the institutional investment in Early Stage Investigators.

Commitment to New and Early Stage Investigators (http://grants.nih.gov/grants/new_investigators/index.htm)

- The 398 Face Page checkbox for “new investigator” is eliminated. The status of new and early stage investigators will be determined electronically from information entered into the eRA Commons Personal Profile.
- Personal Data Form page is eliminated. Information will be collected in the eRA Commons Personal Profile.
- New and early stage investigator policies are described in Part III, 1.15.

Implementation of NIH Reform Act of 2006 (P.L. 109-482)

- One-time eRA Commons Registration requirement is implemented for all individuals with a postdoctoral role and one month or more of measurable effort. The definition of postdoctoral scholar is added.
- Table 12A, required for institutional research training applications, is modified to collect data on percentage of students who successfully attain a doctoral degree and average time to receive a doctoral degree.
- A new Assurance for Institutions Receiving Awards for Training of Graduate Students for Doctoral Degrees is required, as applicable (Part III, 2.16).

Transition of CDAs and Institutional Research Training Applications to Electronic Submission

- The Career Development Awards (CDA or "K" programs, with the exception of K12s) transitioned to electronic submission in February, 2009. CDA application instructions are now included as Part 1, Section 7 of the SF424 (R&R) Application Guide for NIH and Other PHS Agencies.
- The Institutional Research Training Application Including Ruth L. Kirschstein - NRSA Applications transitioned to electronic submission for the January 25, 2010 application receipt date. Instructions for such applications are now included at Part 1.Section 8 of the SF424 (R&R) Application Guide for NIH and Other PHS Agencies.

Important Reminders for all Applicants

Font and margin specifications must be followed; if not, application processing may be delayed or the application may not be reviewed. NIH requires the use of one of four approved fonts and a font size of 11 points or larger. The approved font options include two serif fonts (Palatino and Georgia) and two sans serif fonts (Arial and Helvetica). A symbol font may be used to insert Greek letters or special characters; the font size requirement still applies. A smaller font size may be used for figures, graphs, diagrams, charts, tables, figure legends, and footnotes, but this type must follow the font typeface requirement and be readily legible.

Prepare a *succinct* Research Plan and follow the Table of Page Limits unless the FOA specifies otherwise. Sections 4-15 of the Research Plan have no maximum allowable pages, but should also be succinct.

Several elements of an application are not required at the time the application is submitted. This information is requested later in the review cycle (i.e., just-in-time) to ensure that it is current. See Just-In-Time Policy in Part III. 1.7.

1.1 Application Guide Format

This edition of the PHS 398 is organized into three parts, and is available in two different formats: MS Word and PDF. Within each Part are links to pertinent sections of the application, other documents, or NIH web pages. To use these links in the MS Word version effectively, you must enable the "web" tool bar in order to have a "back button" to return to a page after using a link. The three parts of the 398 are described below:

Part I: Instructions for Preparing and Submitting an Application

Part I includes instructions on submitting a grant application, completing the PHS 398 forms and format pages, preparing the cover letter, Research Plan, and checklist, and information on the peer review process.

Part II: Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan

Part II includes instructions for research that proposes to involve human subjects, including scenarios and detailed instructions to complete Items 6-9 of the Research Plan (Human Subjects Research).

Part III: Policies, Assurances, Definitions and Other Information

Part III includes information on policies, assurances, definitions, and other information relating to submitting applications to the PHS. Applicants should refer to this document as well as the PHS 398 instructional materials, Grants Information (GrantsInfo), and the relevant Grants Policy Statement for additional sources of information. The NIH Grants Policy Statement applies to all NIH awardees; other PHS agencies use the HHS Grants Policy Statement.

Form pages are available ***separately*** on the NIH website (**http://grants.nih.gov/grants/funding/phs398/phs398.html#forms**).

THESE INSTRUCTIONS AND APPLICATION FORMS (Revised xx/2009) SUPERSEDE ALL PREVIOUS EDITIONS. Carefully read the instructions. Submission of an application that fails to meet the PHS requirements will be grounds for the PHS to delay the review or to return the application without peer review. A properly prepared application will facilitate the administrative processing and peer review that must occur before an award can be made.

While the instructions are generally applicable, grant programs of PHS agencies other than NIH may have additional specific instructions. Applicants should contact an official listed in the **table** of PHS agencies to obtain the most current information and instructions.

1.2 NIH Extramural Research and Research Training Programs

The NIH Office of Extramural Research is the focal point for policies and guidelines for extramural research grants administration (http://grants.nih.gov/grants/oer.htm).

The Division of Extramural Outreach and Information Resources (DEOIR) is the central source for general information about NIH extramural research and research training programs, funding activity codes, the peer review system, and application procedures. Grants Information (GrantsInfo) may be contacted by e-mailing GrantsInfo@nih.gov, or calling (301) 435-0714.

1.3 Research Grant Programs and Program Guidelines

A partial list of research grant programs that use the paper PHS 398 Grant Application is provided below, however, not all awarding components use all programs. For a complete listing of program guidelines, visit the OER Grants website http://grants.nih.gov/grants/funding/funding_program.htm. As grant programs transition to electronic submission through Grants.gov using the SF 424 (R&R) they will no longer use this paper PHS 398 application. See http://era.nih.gov/ElectronicReceipt/strategy_timeline.htm for the latest information on the transition to electronic submission.

Research Program Projects and Centers:

- Program Project Grant (P01)
- Exploratory Grants (P20)
- Center Core Grants (P30)
- Biotechnology Resource Grants (P41)

- Research Center Grant (P50)
- Comprehensive Center (P60)

Other Grant Programs

- Research Centers in Minority Institutions (G12)
- Resource-Related Research Projects (R24, U24)

1.4 Interactions with PHS Staff

The PHS agencies encourage applicants to communicate with staff throughout the entire application, review and award process. Web site addresses and phone numbers of relevant NIH awarding components and other PHS agencies are listed in the table below. The non-NIH agencies listed below use this application form, but some have application requirements that differ from NIH. For specific instructions for AHRQ, CDC, FDA and IHS, refer to the links provided below and the terms and conditions of the Notice of Award.

All inquiries regarding the assignment, review, or recommendation on funding of applications are to be made only to PHS officials.

PHS Agency Contacts

PHS AGENCY (LINK TO WEB SITE)	AWARDING COMPONENT (LINK TO WEB SITE)	TELEPHONE NUMBER
NATIONAL INSTITUTES OF HEALTH (NIH)	*Eunice Kennedy Shriver* National Institute of Child Health and Human Development	301-496-0104
NIH	Fogarty International Center	301-496-1653
NIH	National Cancer Institute	301-496-3428
NIH	National Center for Complementary and Alternative Medicine	301-496-4792
NIH	National Center on Minority Health and Health Disparities	301-402-1366
NIH	National Center for Research Resources	301-496-6023
NIH	National Eye Institute	301-451-2020
NIH	National Heart, Lung, and Blood Institute	301-435-0260
NIH	National Human Genome Research Institute	301-496-7531
NIH	National Institute on Aging	301-496-9322
NIH	National Institute on Alcohol Abuse and Alcoholism	301-443-4375
NIH	National Institute of Allergy and Infectious Diseases	301-496-7291
NIH	National Institute of Arthritis and Musculoskeletal and Skin Diseases	301-594-2463
NIH	National Institute of Biomedical Imaging and Bioengineering	301-451-4792
NIH	National Institute on Deafness and Other Communication Disorders	301-496-1804
NIH	National Institute of Dental and Craniofacial Research	301-594-4800

PHS AGENCY (LINK TO WEB SITE)	AWARDING COMPONENT (LINK TO WEB SITE)	TELEPHONE NUMBER
NIH	National Institute of Diabetes and Digestive and Kidney Diseases	301-594-8834
NIH	National Institute on Drug Abuse	301-443-2755
NIH	National Institute of Environmental Health Sciences	919-541-7723
NIH	National Institute of General Medical Sciences	301-594-4499
NIH	National Institute of Mental Health	301-443-3367
NIH	National Institute of Neurological Disorders and Stroke	301-496-9248
NIH	National Institute of Nursing Research	301-594-6906
NIH	National Library of Medicine	301-496-4621
NIH	Center For Scientific Review	301-435-0715
AGENCY FOR HEALTHCARE RESEARCH AND QUALITY	Agency for Healthcare Research and Quality	301-427-1447
CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)	Coordinating Center for Health Information and Services	404-498-1186
CDC	Coordinating Center for Infectious Disease	404-639-3770
CDC	Coordinating Center for Environmental Health & Injury Prevention	770-488-4668
CDC	Coordinating Center for Health Promotion	770-488-8390
CDC	Office of Public Health Research	404-639-4621
CDC	National Institute for Occupational Safety and Health	404-498-2530
CDC	Procurement and Grants Office	770-488-2700
FOOD AND DRUG ADMINISTRATION	Food and Drug Administration	301-827-7185
INDIAN HEALTH SERVICE	Indian Health Service	301-443-0578
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY	Agency for Toxic Substances and Disease Registry	404-842-6630
OFFICE OF PUBLIC HEALTH AND SCIENCE	Office of Population Affairs	301-594-4004
OFFICE OF PUBLIC HEALTH AND SCIENCE	Office of Family Planning	301-594-4008

BEFORE SUBMISSION

Applicants may contact NIH staff with a variety of questions before submitting an application.

- Contact GrantsInfo at (301) 435-0714 or email GrantsInfo@nih.gov, and/or the Division of Receipt and Referral in the Center for Scientific Review (CSR) at (301) 435-0715:
    - To identify Institutes/Centers (ICs) at NIH or other non-NIH agencies, and/or a Scientific Review Group (SRG), that might be appropriate for the application. Note that requests for assignment to an IC and/or a SRG may be made in a cover letter at the time of application submission.

    - To learn about grant programs.
    - To receive advice on preparing and submitting an application (e.g., format, structure).
- Contact program staff in the relevant awarding component:
    - To determine whether a proposed application topic would fit into the NIH IC or other non-NIH agency's programmatic area.
    - To learn about programmatic areas of interest to the IC or other non-NIH agencies.
    - To find out about requesting an assignment to an IC.
    - To discuss responding to a Request for Applications.
- Contact Scientific Review Officers (SRO) in the Center for Scientific Review to discuss requesting assignment to a CSR SRG.

AFTER SUBMISSION

If the initial assignment to an IC or SRG seems inappropriate, the Program Director/Principal Investigator (PD/PI) may request reassignment. Such requests should be made in writing to:

Division of Receipt and Referral
Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Suite 2030, MSC 7720
Bethesda, MD 20892-7720
Fax requests (301-480-1987) are also acceptable.

Although these requests will be carefully considered, the final determination will be made by the PHS agency.

Applicants must never contact reviewers regarding their applications because discussion of the scientific content of an application or an attempt to influence review outcome will create serious breaches of confidentiality in the review process. Reviewers are required to notify the Scientific Review Officer if they are contacted by an applicant. Communication by the applicant to a reviewer may delay the review or result in the return of the application without review.

AFTER ASSIGNMENT

Contact the SRO to discuss the review assignment, to request permission to send additional/corrective materials, and/or to discuss any review concerns (e.g., expertise needed on the SRG, conflicts, reviewers that may have bias).

AFTER PEER REVIEW

Feedback to applicants is very important. Once the PD/PI reviews the Summary Statement in the eRA Commons, the appropriate awarding component program official (noted in the Summary Statement) may be contacted:

- To discuss the review outcome of the application and obtain guidance.
- To get feedback and answers to any questions about the Summary Statement.
- To find out the meaning of a numerical designation pertaining to human subjects or vertebrate animals on the Summary Statement.
- To find out the funding status of an application.

The Peer Review Outcome Letter and Summary Statement will not be mailed to the PD/PI and may only be accessed through the eRA Commons.

1.5 Grants Policy Statements

The *NIH Grants Policy Statement* serves as a term and condition of award and is a compilation of the salient features of policies and various policy issues regarding the administration of NIH awards.

The *HHS Grants Policy Statement* serves as a term and condition of award and is a compilation of the salient features of policies and various policy issues regarding the administration of grant awards from other PHS agencies, excluding NIH awards.

1.6 References

Applicants New to NIH: Getting Started

http://grants.nih.gov/grants/useful_links.htm

Award Information and Data

http://report.nih.gov
Research Portfolio Online Reporting Tool (RePORT)

Contact Information for an NIH Staff Person

http://ned.nih.gov
NIH locator: 301-496-4000

eRA Commons

https://commons.era.nih.gov/commons/index.jsp

Institutions and Program Directors/Principal Investigators (PD/PIs) are required to register with the eRA Commons. Registered PD/PIs can check assignment/contact information, review outcome, and other important information.

Email the Commons Help Desk at commons@od.nih.gov.

Call the Commons Help Desk at 1-800-504-9552 (toll-free) or 301-402-7469; 301-451-5939 (TTY). Business hours are M-F 7am-8pm Eastern Time.

Grant Writing Tips and Sample Applications

http://grants.nih.gov/grants/grant_tips.htm

Grants Information

http://grants.nih.gov/grants/giwelcome.htm
E-mail: GrantsInfo@nih.gov
Telephone: 301-435-0714; 301-451-5936 (TTY)

NIH Office of Extramural Research Human Subjects Website

http://grants.nih.gov/grants/policy/hs/index.htm

This site provides DHHS and NIH requirements and resources for the extramural community involved in human subjects research.

Office of Biotechnology Activities (OBA)

http://www4.od.nih.gov/oba

NIH Guidelines for Research Involving Recombinant DNA Molecules and Institutional Biosafety Committee Registration
Telephone: 301-496-9838

Office for Human Research Protections (Department of Health and Human Services)

http://www.hhs.gov/ohrp

Information about human subject protections, Institutional Review Boards, and Federal Wide Assurances.
Telephone: 1-866-447-4777 or (301) 496-7005

Office of Laboratory Animal Welfare (OLAW)

http://grants.nih.gov/grants/olaw/olaw.htm

Information about animal welfare policy requirements, Institutional Animal Care and Use Committees (IACUC), and Animal Welfare Assurances.
Telephone: 301-496-7163

Receipt/Referral of an Application

http://www.csr.nih.gov/EVENTS/AssignmentProcess.htm

Division of Receipt and Referral
Center for Scientific Review
Telephone: 301-435-0715
Fax: 301-480-1987

Specific Application: Before Review

Telephone or e-mail the Scientific Review Officer identified for the application in the eRA Commons.

Specific Application: Post Review

Telephone or e-mail the NIH Program Official named in the Summary Statement for the application.

1.7 Authorization

The PHS requests the information described in these instructions pursuant to its statutory authorities for awarding grants, contained in Sections 301 (a) and 487 of the PHS Act, as amended (42 USC 241a and 42 USC 288). Therefore, such information must be submitted if an application is to receive due consideration for an award. Lack of sufficient information may hinder the ability of the PHS to review an application and to monitor the grantee's performance.

1.7.1 Collection of Personal Demographic Data

Federal Agencies have a continuing commitment to monitor the operation of its review and award processes to detect, and deal appropriately with, any instances of real or apparent inequities. In addition, section 403 of the 2007 NIH Reform Act requires NIH to report to Congress specifically on postdoctoral individuals supported on research grants; and section 489 of the PHS Act requires NIH

to perform a continuing assessment of research personnel needs. Personal demographic data on PD/PIs and those with a postdoctoral role is vital to comply with these requirements.

NIH collects personal data through the eRA Commons Person Profile. The data is provided one-time by the individual through a secure, electronic system, is confidential, and is maintained under the Privacy Act record system 09-25-0036, "Grants: IMPAC (Grant/Contract Information)." When completing the data entry in the Commons Personal Profile, the individual is responsible for providing true, accurate, and complete data. All analyses conducted on date of birth, citizenship, gender, race, ethnicity, disability, and/or disadvantaged background data will report aggregate statistical findings only and will not identify individuals. Declining to provide information does not affect consideration of an application; however, for some programs (e.g., Ruth L. Kirschstein National Research Service Awards and Research Career Development Awards) citizenship data is required to determine eligibility.

The PHS also requests the last four digits of the Social Security Number (SSN) for accurate identification of individuals and for management of PHS grant programs. Please be aware that no individual will be denied any right, benefit, or privilege provided by law because of refusal to disclose this portion of the SSN. The PHS requests the last four digits of the SSN under Sections 301(a) and 487 of the PHS Act as amended (42 U.S.C. 241a and U.S.C. 288).

1.8 Paperwork Burden

The PHS estimates that it will take approximately 35 hours to complete this form. This estimate excludes time for development of the scientific plan. Other items such as human subjects are cleared and accounted for separately, and therefore are not part of the time estimate. An agency may not conduct or sponsor the collection of information unless it displays a currently valid OMB control number. Nor is a person required to respond to requests for the collection of information without this control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Office, 6705 Rockledge Drive MSC 7974, Bethesda, MD 20892-7974, ATT: PRA (0925-0001). Do not send applications or any materials related to training or career award applications to this address.

2. General Instructions

2.1 Introduction

Read all of the instructions thoroughly prior to application preparation.

These instructions pertain to applications for research project grants that have not transitioned to electronic submission using the SF424 (R&R).

For other specialized grants or cooperative agreements, request additional instructions from the appropriate NIH awarding component or other PHS agency. Phone numbers for contacting the appropriate staff are listed in the Agency Contact Table. For further assistance, contact:

GrantsInfo
National Institutes of Health (NIH)
E-mail: GrantsInfo@nih.gov
Phone: 301-435-0714

Read and follow the instructions carefully to avoid delays, misunderstandings and possible return of the application. Adherence to font and margin requirements is necessary for several reasons. No

applicant should have an advantage over other applicants by providing more content using smaller, denser type. Small type sizes may also make it difficult for reviewers to read the application.

The NIH Center for Scientific Review (CSR), Division of Receipt and Referral, has the responsibility to make the final determination of legibility and the authority to return applications. This decision is final and not subject to appeal. Inquiries should be directed to the:

CSR, Division of Receipt and Referral
Phone: 301-435-0715; TTY 301-451-5936; Fax: 301-480-1987

2.2 Registration Processes

2.2.1 (Reserved)

2.2.2 DUNS Registration for the Applicant Organization & Subaward/Consortium Organizations

A Data Universal Numbering System (DUNS) number is required for all applications (paper and electronic) and must be obtained by the organization prior to submission. For organizations that already have multiple DUNS numbers, one DUNS number should be selected by an authorized organizational representative (AOR) and used consistently for all application submissions. The authorized organizational representative should be consulted to determine the appropriate number to use for applications.

The DUNS number is considered the Federally-recognized unique identifier and is used for reporting purposes, particularly those associated with the *Federal Financial Assistance Transparency Act (FFATA) of 2006* (P.L. 109-282).

FFATA also includes a requirement for reporting on subaward information. Therefore an accurate DUNS number for each subaward/consortium organization must also be provided as part of the Project/Performance Site information.

Additional information on DUNS registration is found at:
http://fedgov.dnb.com/webform/displayHomePage.do

A DUNS number is required for Central Contractor Registration (see 2.2.3. below).

2.2.3 Central Contractor Registration (CCR) for the Applicant Organization

Prior to submission of all applications (paper and electronic), applicant organizations are required to be registered in the Central Contractor Registration (CCR). Organizations must maintain the currency of the information in the registry and renew the registration annually. A DUNS number is required for CCR registration.

CCR is a government-wide registry for organizations doing business with the U.S. Government. The registry collects, validates, stores, and disseminates data in support of agency acquisition missions, including Federal agency contract and assistance awards. The CCR registry will be used by Federal agencies to validate the DUNS number provided as part of the application process. Validation of the DUNS number will be critical for agencies to comply with the requirements of the *Federal Financial Assistance Transparency Act (FFATA) of 2006* (P.L. 109-282).

Organizational information entered into the CCR must match that in the eRA Commons. Since CCR Registration can take several days to complete, the process should be started well in advance of a submission date to avoid potential delays. An authorized organizational representative should be

consulted to determine if the organization has properly completed and maintained CCR registration. Additional information on CCR registration is found at: http://www.ccr.gov/.

2.2.4 eRA Commons Registration

The applicant organization, all PD/PI(s), and all individuals with a postdoctoral role (see definition of postdoctoral scholar in Part III.3) and one month or more of measurable effort, must complete a **one-time** registration in the eRA Commons. Access to the Commons is vital for all steps in the process after application submission. An organization and PD/PIs must be registered in the Commons for purposes of retrieval of grant information, institute/center assignments, review outcomes, and Summary Statements. Institutional/organizational officials are responsible for registering PD/PIs and individuals with a postdoctoral role in the eRA Commons. PD/PIs and individuals with a postdoctoral role should work with their AOR (also known as the Signing Official, or SO, in the eRA Commons) to determine their institutional/organizational process for registration.

IMPORTANT: The eRA Commons registration process should be started at least **two (2) weeks** prior to submission. A valid PD/PI Commons user name ID must be entered in item 3.h of the Face Page. Commons user name IDs for those with a postdoctoral role are not required at the time of application submission, but are required as part of the Non-Competing Continuation Progress Report (PHS 2590).

2.2.4.1 Commons Registration for the Organization

Organizations may verify their current registration status by accessing the "List of Grantee Organizations Registered in NIH eRA Commons" (http://era.nih.gov/userreports/ipf_com_org_list.cfm).

To register an Organization in the eRA Commons:

1. Open the eRA Commons homepage (https://commons.era.nih.gov/commons/).
2. Click Grantee Organization Registration (found in "About the Commons" links on the right side of the screen).
3. Follow the step-by-step instructions. Remember to fax in the registration signature page to eRA.
4. Click Submit. The organization is registered when the NIH confirms the information and sends an email notification of registered Signing Official (SO) account (userid/password).

Organizational data elements, such as Institutional Profile Number (IPF), Entity Identification Number (e.g., 5555555555A5) and DUNS Number must be accurately identified. **Note the DUNS number must be included in the Institutional Profile, and must match the number on the application.**

Since eRA has not required a DUNS number during eRA Commons registration, many accounts do not contain valid information in this field. Prior to submission, the Authorized Organizational Representative/SO should verify that the organization's eRA Commons profile contains the valid DUNS number that will be used for the submission process. The SO has the ability to edit this field in the organization profile in Commons.

To confirm that the organization has a DUNS number or to find out if the DUNS number you have matches the one in the Commons, access the List of Grantee Organizations Registered in NIH eRA Commons (http://era.nih.gov/userreports/ipf_com_org_list.cfm). This listing of grantee organizations registered in Commons and their DUNS numbers can be accessed without logging into Commons.

2.2.4.2 Commons Registration for the Project Director/Principal Investigator (PD/PI) and Individuals with a Postdoctoral Role

The individual(s) designated as the PD/PI(s) on the application must be registered in the Commons. The PD/PI must hold a PI account **and** be affiliated with the applicant organization. **This registration**

must be done by an organizational official (or delegate) who is already registered in the Commons. To register PD/PIs in the Commons, refer to the NIH eRA Commons System Users Guide (http://era.nih.gov/Docs/COM_UGV2630.pdf).

Once the PD/PI has received email confirming his/her registration within the Commons, the PD/PI must verify that all Personal Information located within the Personal Profile tab in the eRA Commons System is accurate. Please have the PD/PI review and update, as needed, data elements such as first name, middle initial, last name, prefix and/or suffix to PD/PI name (including all embedded punctuation), email, phone, fax, street address, city, state, country, zip and degrees earned. The PD/PI must enter the date of his/her terminal research degree, or end date of medical residency, to receive consideration as an Early Stage Investigator. All data must contain the most recent information in order for the application to be processed accurately.

Both PD/PI and SO need separate accounts in Commons since both must verify the application. If you are the SO for your organization as well as a PI of the grant, you will need two separate accounts with different user names – one with SO authority and one with PI authority. When an organization is registered, an SO account is created. Log on to the account with the SO authority role and create another account with PI authority.

Individuals with a postdoctoral role and one month or more of effort must also be registered in the eRA Commons and should verify that all Personal Information located within the Personal Profile tab in the eRA Commons System is accurate. The Commons user name ID for those with a postdoctoral role is not required at the time of application submission, but will be required as part of the Non-Competing Continuation Progress Report (PHS 2590).

2.3 (Reserved)

2.4 Funding Opportunities

Grants for health-related research and research training projects or activities make up the largest category of funding provided by the NIH Institutes/Centers (ICs) and other non-NIH agencies. Most applications for support are **unsolicited** and originate with individual investigators who develop proposed plans for research or research training within an area that is relevant to the NIH. Research project grants are awarded to organizations/institutions on behalf of PD/PIs to facilitate the pursuit of a scientific objective when the idea for the research is initiated by the investigator. If the funding agency anticipates substantial program involvement during the conduct of the research, a cooperative agreement will be awarded, rather than a grant. The NIH awards grants and cooperative agreements for terms ranging from one to five years. Organizational/institutional sponsorship assures that the awardee organization will provide the facilities and the financial stability necessary to conduct the research, and be accountable for the funds. For a list and brief description of grant activity codes, see Part III, 4.1.

2.4.1 NIH Guide for Grants and Contracts

The *NIH Guide for Grants and Contracts*, a weekly electronic publication (http://grants.nih.gov/grants/guide), contains announcements about funding opportunities, such as Requests for Applications (RFAs) and Program Announcements (PAs), including Parent Announcements, from NIH and other PHS agencies. The *NIH Guide* also contains vital information about policies and procedures. To subscribe to the *NIH Guide*, visit http://grants.nih.gov/grants/guide/listserv.htm.

2.4.2 Funding Opportunity Announcements (FOAs)

To hasten the development of a program or to stimulate submission of applications in an area of high priority or special concern, an awarding component will encourage applications through the issuance of a PA to describe new, continuing, or expanded program interests, or issuance of an RFA inviting applications in a well-defined scientific area to accomplish a scientific purpose.

Definitions are as follows:

Parent Announcements: Electronic grant applications must be submitted in response to a Funding Opportunity Announcement (FOA). For applicants who wish to submit what were formerly termed "investigator-initiated" or "unsolicited" applications, NIH and other PHS agencies have developed Parent Announcements. Responding to such an omnibus or umbrella Parent FOA ensures that the correct application package is used and enables NIH to receive the application from Grants.gov. Additional information about, as well as links to published Parent Announcements, can be found at: http://grants.nih.gov/grants/guide/parent_announcements.htm.

Program Announcement (PA): A formal statement about a new or ongoing extramural activity or program. It may serve as a reminder of continuing interest in a research area, describe modification in an activity or program, and/or invite applications for grant support. Most applications in response to PAs may be submitted to a standing submission date and are reviewed with all other applications received at that time.

Request for Applications (RFA): A formal statement that solicits grant or cooperative agreement applications in a well-defined scientific area to accomplish specific program objectives. An RFA indicates the estimated amount of funds set aside for the competition, the estimated number of awards to be made, and the application submission date(s). Applications submitted in response to an RFA are usually reviewed by a Scientific Review Group (SRG) specially convened by the awarding component that issued the RFA.

PAs (including Parent Announcements) and RFAs are published in the *NIH Guide for Grants and Contracts* (http://grants.nih.gov/grants/guide), the *Federal Register* (http://www.gpoaccess.gov/nara/index.html), and on Grants.gov under Find Grant Opportunities (http://www.grants.gov/applicants/find_grant_opportunities.jsp). Read the announcement carefully for special instructions. The instructions in the announcement may differ from these general instructions, and the instructions in the announcement **always** supersede these general instructions. Each announcement published in the *NIH Guide for Grants and Contracts*, the *Federal Register*, Grants.gov Find, or other public document contains contact information under *Inquiries* in addition to information specific to the announcement.

While individual announcements will continue to carry an announcement number reference to "PA" or "RFA", all announcements are "Funding Opportunity Announcements (FOAs)." This general term will be used to reference any type of funding announcement. NIH will continue to use the PA and RFA references in the actual announcement number to distinguish between the various types of announcements.

2.5 (Reserved)

2.6 Format Specifications

Follow font and format specifications. Otherwise, application processing may be delayed or the application may not be reviewed.

Font

- Use an *Arial, Helvetica, Palatino Linotype or Georgia typeface, a black font color, and a font size of 11 points or larger*. A symbol font may be used to insert Greek letters or special characters; the font size requirement still applies.
- Type density, including characters and spaces, must be no more than 15 characters per inch.
- Type may be no more than six lines per inch.
- Use black ink that can be clearly copied.
- Print must be clear and legible.

Paper Size and Page Margins

- Use standard size *(8 ½" x 11")* sheets of paper.
- Use at least one-half inch margins (top, bottom, left, and right) for all pages, including continuation pages. No information should appear in the margins, including the PD/PI's name and page numbers.

Page Formatting

- Because a number of reviewers will be reviewing applications as electronic documents and not paper versions, applicants are strongly encouraged to use only a standard, single-column format for the text. Avoid using a two-column format since it can cause difficulties when reviewing the document electronically.
- The application must be single-sided and single-spaced.
- Consecutively number pages throughout the application. Do not use suffixes (e.g., 5a, 5b).
- Do not include additional pages between the face page and page 2.
- Do not include unnumbered pages.

Figures, Graphs, Diagrams, Charts, Tables, Figure Legends, and Footnotes

- A smaller type size is acceptable, but it must be in black ink, readily legible, and follow the font typeface requirement.

Grantsmanship

- Use English and avoid jargon.
- If terms are not universally known, spell out the term the first time it is used and note the appropriate abbreviation in parentheses. The abbreviation may be used thereafter.

Photographs and Images

- Do not include photographs or other materials that are not printed directly on an application page in the body of the application. Pictures or other materials that are glued or taped onto application pages are incompatible with the current duplication/scanning process.
- You may include black-and-white or color images in the six (6) submitted copies provided such images are printed directly on the application page and are critical to the content of the application.

Copies

- Send the original application (signed by an authorized organizational official) and five identical, legible, single-sided photocopies.

- Do not use photo reduction.
- The application must contain only material that reproduces well when photocopied in black and white. Glossy photographs or other materials that cannot be photocopied must be submitted in the appendix (see Section 5.7). *Note:* Photographs may be included in the appendix; however, a photo copy of each must also be included within the page limits of the Research Strategy.

Page Limits

All applications for NIH funding must be self-contained within specified page limits.

Observe the page number limits provided in the table below, unless the FOA specifies otherwise. Page limits for activity codes not listed below should follow the page limits specified in the FOA.

SECTION OF APPLICATION Also refer to the relevant section of the application instructions and the FOA.	**PAGE LIMITS ***
Introduction to Revision or Resubmission Applications	1 page
Introduction to Revision or Resubmission Applications For each project and core of multi-component applications	1 page
Specific Aims	1 page
Research Strategy (Item 5.5.3 of Research Plan) For Activity Codes R03, R13/U13, R21, R36, R41, R43, Fellowships (F), SC2, SC3	6 pages
Research Strategy (Item 5.5.3 of Research Plan) For Activity Codes R01, single project U01, R10, R15, R18, U18, R21/R33, R24, R33, R34, U34, R42, R44, DP3, G08, G11, UH2, UH3, SC1, X01	12 pages
Research Strategy (Item 5.5.3 of Research Plan) For all other Activity Codes, including Cs, Ps, Ss, Ts, Us, etc.	follow FOA instructions *
Biosketch (per person) For all Activity Codes except DP1 and DP2	4 pages
Biosketch (per person) For DP1 and DP2	2 pages
Appendix	No page limits, but content limitations. See relevant section of instructions and FOA

*** FOA instructions always supersede these instructions.**

2.7 Resubmission Applications

For all original new (i.e. never submitted) and competing renewal applications submitted for the January 25, 2009 due date and beyond, NIH will accept only a single amendment (A1) to the original application (called a resubmission application).There is no time limit for a resubmission application. Any second resubmission will be administratively withdrawn and not accepted for review. For original new and competing applications submitted prior to January 25, 2009, applicants are permitted two

resubmissions (A1 and A2). For these “grandfathered” applications, any second resubmission (A2) must be submitted no later than January 7, 2011, and NIH will not accept any A2 resubmissions after that date. See NIH Policy on Submission of a Revised/Resubmission (amended) Application in Part III,1.3.

NIH has established new policies for application resubmissions of certain categories. See Resubmission of Unpaid RFA Applications and Resubmission of Applications with a Changed Grant Activity Code in Part III, 1.2.

There are four requirements for a Resubmission application:

- The Summary Statement must be available in the eRA Commons (http://commons.era.nih.gov/commons/)
- The PD/PI(s) must make significant changes to the application.
- An Introduction must be included that summarizes the substantial additions, deletions and changes to the application. The Introduction must also include a response to the issues and criticism raised in the Summary Statement. Use the Introduction to Application of the Research Plan (see 5.5.1) to provide this information. The Introduction may not exceed one page, unless the FOA specifies otherwise.
- The substantial scientific changes must be marked in the text of the application by bracketing, indenting, or changing typography. Do not underline or shade the changes. Deleted sections should be described but not marked as deletions. If the changes are so extensive that essentially all of the text would be marked, explain this in the Introduction. The Research Strategy/Progress Report section (see 5.5.3.c) should incorporate work completed since the prior version of the application was submitted.

See NOT-OD-07-083 for special conditions and due dates for new investigator resubmission applications submitted for consecutive review cycles. Note this applies only to new investigator R01s submitted for standard receipt dates and reviewed in recurring SRGs in CSR, and selected other study sections only (e.g., NOT-MH-08-002).

Acceptance of a resubmission application will not automatically withdraw the prior version. eRA keeps all versions (e.g., 01, A1) of a grant application active and provides an internal Multiple Active Applications (MAA) flag for each application in an active cluster. The cluster allows applicants to identify quickly all versions of one application. If any version in a cluster is awarded, all other applications within the cluster will be automatically withdrawn without any additional action by applicants or staff.

Investigators who have submitted multiple versions of an application and have not been successful often ask NIH what constitutes a “new application.” It is recognized that investigators are trained in a particular field of science and are not likely to make drastic changes in their research interests. However, a new application following multiple reviews is expected to be substantially different in content and scope with more significant differences than are normally encountered in a Resubmission application. Simply rewording the title and Specific Aims or incorporating minor changes in response to comments in the previous Summary Statement does not constitute a substantial change in scope or content. Changes to the Research Plan should produce a significant change in direction and approach for the research project. Thus, a new application would include substantial changes in all sections of the Research Plan, particularly the Specific Aims and the Research Strategy sections.

In the referral process, NIH staff look at all aspects of the application, not just the title and Project Summary. 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. If identified after assignment or review, identical applications will be withdrawn.

2.8 Revision Application

A Revision application (formerly called a competing supplement) may be submitted to request support for a significant expansion of a project's scope or research protocol. Revision applications are not appropriate when the sole purpose is to restore awards to the full SRG-recommended level if they were administratively reduced by the funding agency. **A Revision application must not be submitted until after the original application has been awarded and must not extend beyond the term of the current award period.**

Introduction: Provide a one-page introduction at the beginning of the Research Plan (see 5.5.1) that describes the nature of the revision and how it will influence the Specific Aims and Research Strategy of the current grant. The body of the application should contain sufficient information from the original grant application to allow evaluation of the proposed revision in relation to the goals of the original application. Note that all revision applications must be submitted by the same PD/PI (or contact PD/PI for multi-PI grants) as listed on the current award and applicants must use the same budget format as the current award. Any budgetary changes for the remainder of the project period of the current grant should be discussed under the budget justification.

If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the SRG, then the applicant must respond to the criticisms in the prior Summary Statement, and substantial changes must be clearly evident and summarized in the Introduction.

Administrative Supplements

An administrative supplement provides additional funding to meet increased costs that are within the scope of an approved application, but that were unforeseen when the new or competing Renewal application was submitted. If considering administrative supplemental funding, consult in advance with the designated Grants Management Officer and Program Official. It is important to submit a request before the grant expires. To be considered for an administrative supplement, submit a request in writing to the Institute/Center, not to the Division of Receipt and Referral, Center for Scientific Review. The request must be signed by the authorized Business Official and describe the need for additional funding and the categorical costs. In the letter, point out what will NOT be accomplished if such a request is denied. Administrative supplements may **not** be submitted using the 398 Application.

2.9 Similar, Essentially Identical, or Identical Applications

Submissions of identical applications to one or more components of the PHS are not allowed, and the NIH will **not** accept similar grant applications with essentially the same research focus from the same applicant organization. This includes derivative or multiple applications that propose to develop a single product, process or service that, with non-substantive modifications, can be applied to a variety of purposes. Likewise, identical or essentially identical grant applications submitted by different applicant organizations will not be accepted. Applicant organizations should ascertain and assure that the materials they are submitting on behalf of the PD/PI are the original work of the PD/PI and have not been used elsewhere in the preparation and submission of a similar grant application. Applications to the NIH are grouped by scientific discipline for review by individual Scientific Review Groups. The reviewers can thus easily identify multiple grant applications for essentially the same project. In these cases, application processing may be delayed or the application(s) may not be reviewed.

Essentially identical applications will only be reviewed in the following circumstances: 1) an application for an Independent Scientist Award (K02) proposing essentially identical research in an application for a research project; and 2) an application for a research project identical to a subproject of a program project or center grant application.

2.10 (Reserved)

2.11 (Reserved)

2.12 (Reserved)

2.13 Submission of Supplementary or Corrective Information

Applicants may need to submit supplementary or corrective material after the submission date, such as revised budget pages, biographical sketches, updated or supplemental pages, letters of support or collaboration and publications (accepted but not yet published, see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-018.html). Acceptance of additional materials prior to peer review is at the discretion of the NIH Scientific Review Officer (SRO). Additional materials should be sent as a PDF attachment to an e-mail. E-mail communication is preferred. If e-mail is not feasible, please send in a hard copy.

The original application is kept intact; any additional material is sent separately to reviewers. Updated or supplemental grant application materials used in the peer review process will be retained as part of the official grant file and remain part of the permanent record for that application.

The additional materials must be submitted to the NIH SRO with the consent of the applicant organization's designated AOR/SO. NIH requires that the applicant organization include the AOR in the correspondence; the AOR is not necessarily required to submit the application materials. It is acceptable for the PD/PI or Contact PI for multiple PD/PI applications to send such materials with the concurrence of the AOR (designated institutional signing official). Materials sent without evidence of such concurrence will not be accepted.

The deadline for receipt of additional materials is one month (30 calendar days) prior to the peer review meeting. FOAs may provide stricter or more lenient guidance.

After the initial peer review phase is completed, the NIH Chief Grants Management Officer is the NIH official responsible for accepting additional materials. Most of the material submitted after the initial peer review can be submitted as part of the Just-in-Time process (see Part III, 1.7).

See also the NIH Best Practice Guidelines for Accepting Additional Grant Application Materials.

2.14 Application Submission Dates

Paper application submission dates fall under two different categories: 1) Standard Postmark/Submission Dates (also known as "send by" dates) and 2) Special Receipt Dates (also known as "arrive by" dates) which are specified in RFAs and PAs.

Applications submitted for the standard submission dates listed at http://grants.nih.gov/grants/dates.htm are considered on time if they are sent on or before the appropriate date listed and a proof of mailing is provided. The critical determination is when the application is sent, not when it arrives at NIH. Proof of timely mailing consists of one of the following: a legibly dated U.S. Postal Service postmark, or a dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks are not acceptable.

Weekend/Federal holiday submission dates. If a submission date falls on a weekend, it will be extended to the following Monday; any time the date falls on a Federal holiday the submission date will be extended to the following business day. The application will be on time if it is sent on or before the following business day.

Funding Opportunity Announcements (RFAs and PARs). Applications in response to announcements with special receipt dates must be received at NIH by the specified date. However, an application received after the deadline may be acceptable if it carries a legible proof-of-mailing date assigned by the carrier not later than 1 week prior to the deadline date. Note that this differs from the procedures for submitting applications for the standard due dates, which are considered submission or "send by" dates.

Modified Submission Policy for Appointed NIH Study Section Members. An alternate submission policy for R01, R21, and R34 applications submitted with appointed members of chartered standing NIH study sections as PD/PIs is available for applications that would normally be received on standard submission dates (not special receipt dates). See NIH Guide Notice OD-08-026.

Late applications. Permission is **not** granted in advance for submission of a late application. Late applications are accepted only in extenuating circumstances. If an application is submitted late, a cover letter explaining the reasons for the delay **must** be included with the signed, completed application. Late applications are evaluated on an individual basis considering the reasons provided. Contacting the Division of Receipt and Referral in advance will not influence the acceptance of a late application. For additional information on late applications, see NIH Guide Notices OD-08-027 and OD-08-111.

2.15 Submission, Review and Award Cycles

The PHS submission, review, and award schedule is provided at this website: http://grants.nih.gov/grants/dates.htm. Note that many activity codes have transitioned to electronic submission and the SF424 (R&R) application and instructions. The PHS 398 should only be used for those activity codes where the Application Form is identified as PHS 398. Applicants should refer to the OER Electronic Submission of Grant Applications website, http://era.nih.gov/ElectronicReceipt/ for details on the transition to electronic submission.

For specialized grant applications, consult with the appropriate PHS agency prior to the preparation of an application.

Application Assignment Information

Competing grant applications submitted to the PHS agencies will be processed through the Division of Receipt and Referral, CSR, unless otherwise stated. Administrative information about the application is entered into a computer system. The application will be assigned to an appropriate Scientific Review Group and awarding component(s). Assignment is based on the scientific content of the application using established referral guidelines. Business rule validations are conducted by NIH staff.

Assignment to Review Group. The Center for Scientific Review (CSR) will assign appropriately completed applications to the Scientific Review Groups (commonly referred to as "SRGs" or "study sections") that will perform the scientific/technical merit review. The CSR lists the recurring review panels (http://cms.csr.nih.gov/PeerReviewMeetings/CSRIRGDescription/), and you may suggest a specific group in the PHS 398 Cover Letter component. See Part I, Section 3.1 for a suggested format for requesting a specific SRG in the Cover Letter.

Assignment to Relevant Potential Awarding Component(s) (ICs). In addition, CSR will assign each application to the agency awarding component that is the potential funding component. When the scientific areas and the research proposed in a grant application are sufficiently relevant to the program responsibilities of two or more awarding components, CSR may assign your application to all such components. The component that has the most relevant program responsibility is designated as

the primary assignee. The other components that have an interest in your application are designated as secondary assignees. If your application is eligible for funding and the primary assignee does not intend to make an award, the secondary assignees will be given the opportunity to do so. Although these suggestions will be taken into consideration, the final determination will be made by the agencies participating in this solicitation.

After the submission date, usually within 2 weeks, the following information regarding the grant application will be available in the NIH eRA Commons for viewing by the PD/PI(s) and an authorized organizational official:

- application assignment number;
- name, address, and telephone number of the Scientific Review Officer of the Scientific Review Group to which the application has been assigned for peer review; and
- assigned Institute/Center information.

If assignment information is not available in the eRA Commons within two weeks of the submission date, contact the Division of Receipt and Referral, Center for Scientific Review (CSR), National Institutes of Health, Bethesda, MD 20892-7720, (301) 435-0715. If there is a change in assignment, you will receive a notification and the change will be reflected in the eRA Commons.

Applicants must **not** communicate directly with any review group member about an application either before or after the review. Failure to strictly observe this policy will create serious breaches of confidentiality in the peer review process. From the time of assignment to the time the review of the application is complete, applicant investigators must direct all questions to the Scientific Review Officer. This individual is in charge of the review group and is identified in the eRA Commons.

2.16 Resources for Finding Help

2.16.1 (Reserved)

2.16.2 Finding Help for the eRA Commons Registration

If help is needed with the eRA Commons registration process for the applicant organization and PD/PIs, contact the eRA Commons Helpdesk:

eRA Commons Helpdesk: http://ithelpdesk.nih.gov/eRA/

eRA Commons Helpdesk Email: commons@od.nih.gov

eRA Commons Phone: 301-402-7469
866-504-9552 (Toll Free)
301-451-5939 (TTY)

The eRA Commons Helpdesk hours of operation are Monday-Friday from 7:00 a.m. to 8:00 p.m. Eastern Time.

2.16.3 Finding Help for Application Preparation

If after reviewing these application instructions, help is needed in preparing the application, contact GrantsInfo:

GrantsInfo Phone: 301-435-0714
301-451-5936 (TTY)

GrantsInfo Email: GrantsInfo@nih.gov

3. Submission of the Grant Application

Submit a complete application. The application must be complete and accurate at the time of submission. Applications may not be reviewed if they are incomplete, illegible, fail to follow instructions, or present insufficient material to permit an adequate review.

There is no guarantee that the Scientific Review Officer will accept or the peer reviewers will consider additional material (see Part I, 2.13 Submission of Supplementary or Corrective Information, and NOT-OD-07-018).

3.1 Cover Letter

Applicants are encouraged to include a cover letter with the application. The letter is only for internal agency use and will not be shared with peer reviewers. Place the letter at the beginning of the original application; do not copy it.

- Application title.
- Funding Opportunity Announcement (PA, RFA or Parent Announcement title, if applicable).
- Request of an assignment (referral) to a particular IC or Scientific Review Group (SRG). While requests are given careful consideration, the PHS makes the final determination for assignments. (See suggested format below.)
- List of individuals (e.g., competitors) who should not review the application and why.
- Disciplines involved, if multidisciplinary.
- Statement that any required NIH approval documentation for the type of application submitted is enclosed. This may include approval for applications requesting $500,000 or more, approval for Conference Grant, Cooperative Agreement, etc.
- For late applications (see Late Application Policy), include an explanation of the delay as part of the cover letter.

Suggested Cover Letter Format

The Division of Receipt and Referral (DRR), Center for Scientific Review (CSR) is responsible for assigning applications to ICs and to Scientific Review Groups (SRGs). DRR will be utilizing knowledge management approaches as an adjunct to the work of referral experts as part of an overall plan to shorten the time from submission to review. Analysis has shown that requests made by investigators are a valuable source of information in this process. In order to facilitate the use of these requests in conjunction with knowledge management analysis of the content of the application, applicants are requested to use the following format when assignment requests are contained in a cover letter.

- List one request per line.
- Place Institute/Center (IC) and SRG review requests (if both are made) on separate lines.
- Place positive and negative requests (if both are made) on separate lines.
- Include name of IC or SRG, followed by a dash and the acronym. Do not use parentheses.
- Provide explanations for each request in a separate paragraph.

Examples:

Please assign this application to the following:

Institutes/Centers

National Cancer Institute - NCI

National Institute for Dental and Craniofacial Research – NIDCR

Scientific Review Groups

Molecular Oncogenesis Study Section – MONC

Cancer Etiology Study Section – CE

Please do not assign this application to the following:

Scientific Review Groups

Cancer Genetics Study Section – CG

The reasons for this request are [provide a narrative explanation for the request(s)].

3.2 Number of Copies

Submit the **original and five** identical, legible, single-sided photocopies of each application. The **original must be signed** by an authorized organizational official.

3.3 Bindings and Packaging

Submit the following materials in *one* package:

- cover letter (original only);
- original application;
- five copies of the application, made after the original has been signed and **not** including the cover letter;
- Appendix materials – five identical CDs of all appendix material in PDF format.

Do not include more than one application (original plus 5 copies and appendices) in each mailing envelope.

Cover letter. Place the original cover letter at the beginning of the original application. It should not be duplicated.

The original application. The original application must be single-sided, with the required signature on the Face Page. Do **not** staple or otherwise bind the original application. Rubber bands or clips are acceptable. Assemble the pages in the order specified in the table of contents.

Five identical, single-sided copies of the original application. Make the copies **after** an authorized organizational official has signed the Face Page so that the official's signature is present on the copies. Do **not** include the cover letter in the copies. Do not staple or otherwise bind the five copies of the original application. Rubber bands or clips are acceptable.

Five identical CDs containing all appendix material. When preparing CDs:

- Use PDF format.
- Label each disk with the PD/PI name and application title.

- If burning CD-ROM disks on a Mac, select the ISO 9660 format.
- Do not use compression techniques for the electronic files.
- Do not use password protection, encryption, digital signature and/or digital certification in the PDF files.

Appendix materials submitted in paper are not accepted and may lead to a delay in the review process.

3.4 Application Mailing Address

For applications to NIH, use the mailing label provided at the end of the forms.

Send the application to the following address, making sure to use the correct ZIP code:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Suite 1040
MSC 7710
Bethesda, MD 20892-7710
(United States Postal Service (USPS) Express or Regular mail)
or
Bethesda, MD 20817 **(Express/Courier Non-USPS Service)**

C.O.D. applications will not be accepted.

All applications and other deliveries to the Center for Scientific Review must come either via courier delivery (e.g., Federal Express, DHL, UPS) or via the USPS. Applications delivered by individuals to the Center for Scientific Review will not be accepted. For additional information, see **http://grants.nih.gov/grants/ guide/notice-files/NOT-OD-03-040.html**.

There may be additional instructions for submission of responses to RFAs; check the FOA for details.

For applications to other (non-NIH) PHS agencies, refer to the FOA for submission instructions and mailing addresses.

4. Completing the PHS 398 Forms and Format Pages

Prepare the application using the PHS 398 MS WORD or PDF form pages and format pages as provided at http://grants.nih.gov/grants/funding/phs398/phs398.html.

- *Form pages* must be identical to those provided. You may substitute computer-generated facsimiles for government-provided forms; however, they must maintain the exact wording and format of the government forms, including all captions and spacing.
- *Format pages* are intended to assist you in the development of specific sections of the application. Alternatively, you may create a page similar to any format provided as long as all the requisite information is included.
- Shading/colors may not be used in any text portions, including the face page.
- Font sizes on some PHS 398 form pages vary due to field or space limitations. The PHS 398 Microsoft Word (MS Word) and Portable Document File (PDF) Form Pages as provided are acceptable to NIH. All other sections of the application (e.g., Biographical Sketch; Introduction, if necessary; and the Research Plan) must conform to the font requirements stated in 2.6 Format Specifications above.

- Some fields on the PDF Form Pages are pre-set to auto calculate. In these cases, a zero will appear until actual data are entered.

4.1 Face Page

The first part of the Face Page (Form Page 1) must be printed on a single page. The Face Page must not have any shading or colors. Form Page 1-continued is only for multi-PD/PI applications; if used, it should be printed as a separate page.

The information provided on the Face Page of the application and the fiscal information, including the calculation of F&A costs, must be verified by the official signing for the applicant organization.

Item 1. Title of Project

Do not exceed 81 characters, including the spaces between words and punctuation. Choose a descriptive title that is specifically appropriate. A new application must have a different title from any other PHS project with the same PD/PI. A Renewal or Resubmission application should normally have the same title as the previous grant or application. If the specific aims of the project have significantly changed, choose a new title. A Revision application **must** have the same title as the currently funded grant.

Item 2. Response to Specific Request for Applications (RFA) or Program Announcement (PA)

Check "Yes" and insert the appropriate announcement number (e.g., PA-06-512) and title of the announcement if the application is submitted in response to an RFA or a PA issued through the NIH Guide for Grants and Contracts.

Item 3. Program Director(s)/Principal Investigator(s) (PD/PI)

Item 3a. Name of Program Director/Principal Investigator (PD/PI)

Name the one person responsible to the applicant organization for the scientific and technical direction of the project. **PHS staff conduct official business only with the named PD/PI and institutional officials.** A Revision application **must** have the same PD/PI as the currently funded grant.

When multiple PD/PIs are proposed, use the Face Page-Continued page to provide items 3a – 3h for all PD/PIs. NIH requires one PD/PI be designated as the "contact PD/PI" for all communications between the PD/PIs and the agency. The contact PD/PI must meet all eligibility requirements for PD/PI status in the same way as other PD/PIs, but has no special roles or responsibilities within the project team beyond those mentioned above. The contact PD/PI may be changed during the project period. The contact PD/PI should be listed in block 3 of Form Page 1 (the Face Page), with all additional PD/PIs listed on Form Page 1-Continued. When inserting the name of the PD/PI in the header of each application page, use the name of the "Contact PD/PI, et. al." The contact PD/PI must be from the applicant organization if PD/PIs are from more than one institution.

All individuals designated as PD/PI must be registered in the eRA Commons and must be assigned the PD/PI role in that system (other roles such as SO or IAR will not give the PD/PI the appropriate access to the application records). Each PD/PI must include his/her respective eRA Commons ID in the eRA Commons User Name field.

Item 3b. Degree(s)

Indicate up to three academic and professional degrees or other credentials, such as licenses (e.g., R.N.).

Item 3c. Position Title

Provide the academic or professional title of the PD/PI. If more than one title, indicate the one most relevant to the proposed project (e.g., Professor of Biochemistry, Chief of Surgical Service, or Group Leader).

Item 3d. Mailing Address

Provide complete information (including room number, building, and street address) necessary for postal delivery. All written communications with the PD/PI will use this address. For electronic mail, enter the appropriate e-mail address (not a website URL).

Item 3e. Department, Service, Laboratory, or Equivalent

Indicate organizational affiliation, such as Department of Medicine, Materials Research Laboratory, or Social Sciences Institute.

Item 3f. Major Subdivision

Indicate school, college, or other major subdivision, such as medical, dental, engineering, graduate, nursing, or public health. If there is no such subdivision, enter "None."

Item 3g. Telephone and Fax Numbers

Provide a daytime telephone number and, if available, a fax number.

Item 3h. eRA Commons User Name

The Commons User Name is the ID assigned to and used by the individual to access the eRA Commons. **All** PD/PIs are required to be registered in the eRA Commons and **must** provide their Commons User Name. The PD/PI must enter the date of his/her terminal research degree, or end date of medical residency, to receive consideration as an Early Stage Investigator. All data must contain the most recent information in order for the application to be processed accurately.

Item 4. Human Subjects Research

No Human Subjects Involved

Check "No" if activities involving human subjects are not planned at any time during the proposed project period. The remaining parts of Item 4 are then not applicable.

Human Subjects Involved

Check "Yes" if activities involving human subjects are planned at any time during the proposed project period, either at the applicant organization or at any other Project/Performance Site or collaborating institution. Check "Yes" if the research is exempt from DHHS regulatory requirements for the protection of human subjects (see Exemption Categories).

If you plan to conduct research involving human subjects, but do not have definite plans at the time of application, you will need to include item 6 of the Research Plan. Certification of IRB review and approval must be provided and accepted by the awarding component before the research may occur.

NIH does not require certification of review and IRB approval of proposed research prior to NIH peer review of an application (see **http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-031.html** and Part II, **Human Subjects Research** supplemental instructions). However, any modification of the Research Plan section of the application required by the IRB or to address human subjects concerns raised during review, must be submitted for approval before award. See also the **Just-In-Time Policy** and **IRB Approval**.

The DHHS regulations "Protection of Human Subjects" (45 CFR Part 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*." See Part III.3 for the definitions of italicized terms used in the definition of human subject.

To help determine whether research that involves the use of human data or biological specimens is human subjects research, refer to http://grants.nih.gov/grants/policy/hs/.

Additional information is available at:

- OHRP Decision Charts: http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm
- OHRP Guidance on Repositories: http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm; http://www.hhs.gov/ohrp/humansubjects/guidance/guid1223.pdf
- OHRP Memo on Engagement: http://www.hhs.gov/ohrp/humansubjects/assurance/engage08.html

Item 4a. Exemptions from Department of Health and Human Services (DHHS) Human Subjects Regulations

Check "Yes" if the activities proposed are exempt from the regulations at 45 CFR Part 46. Insert the exemption number(s) corresponding to one or more of the six exemption categories listed in Part III under Human Subjects Research Definitions and Terms.

OHRP guidance states that appropriate use of Exemptions described in 45 CFR 46 should be determined by an authority independent from the investigators (http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd107.pdf). Institutions often designate their IRB to make this determination. Because NIH does not require IRB approval at the time of application, the exemptions designated in item 4a often represent the opinion of the PD/PI, and the justification provided for the exemption by the PD/PI is evaluated during peer review.

Proposed research may include more than one research project; thus the application may include individual projects that meet the requirements for non-exempt or exempt human subjects research, or are not defined as human subjects research. Human subjects research should be designated as exempt if **all** of the proposed research meets the criteria for one or more of the six exemptions.

Check "No" if any of the planned activities involving human subjects are not exempt, and complete the remaining parts of Item 4.

Item 4b. Human Subjects Assurance Number

If the applicant organization has a current approved Federal Wide Assurance (FWA) on file with the OHRP (http://www.hhs.gov/ohrp/), enter the number in the space provided.

Enter "None" in Item 4b if the applicant organization does not have an approved FWA on file with OHRP. In this case, the signature on the Face Page is a declaration that the applicant organization will comply with 45 CFR Part 46 and proceed to obtain a FWA (see http://www.hss.gov/ohrp).

Do not enter the human subjects assurance number of any Project/Performance Site or collaborating institution in the space provided.

Item 4c. Clinical Trial

Check "Yes" or "No" to indicate whether the project includes a clinical trial. Refer to the definition of "clinical trial" in Part III.3, under Human Subjects Research Definitions and Terms.

Note that Public Law 110-85, enacted 09/27/2007, mandates registration and results reporting of applicable clinical trials in ClinicalTrials.gov (see Part II, 4.1.6 and Part III, 2.1.6).

Item 4d. NIH-Defined Phase III Clinical Trial

Check “Yes” or “No” to indicate whether the project is an NIH-Defined Phase III Clinical Trial. Refer to the definition of "NIH-Defined Phase III Clinical Trial" in Part III.3, under Human Subjects Research Definitions and Terms.

Item 5. Vertebrate Animals

Check “No” if activities involving vertebrate animals are not planned at any time during the proposed project period, and leave item 5a blank. Note that generation of custom antibodies constitutes an activity involving vertebrate animals.

Check “Yes” if activities involving vertebrate animals are anticipated or planned at any time during the proposed project period, either at the applicant organization or at any other Project/Performance Site or collaborating institution. If animal involvement is anticipated within the period of award but plans are indefinite and it is not possible to describe the use of animals, check "Yes" and in the Research Plan, item 12, provide an explanation and indicate when it is anticipated that animals will be used. Before activities with animals begin, the applicant must provide all of the information required by 5.5, Research Plan, item 12, Vertebrate Animals, with verification of current IACUC approval, to the awarding component for prior approval. IACUC approval must have occurred within the past three years to be considered current.

NIH does not require verification of review and approval of the proposed research by the Institutional Animal Care and Use Committee (IACUC) before peer review of the application. However, this information is required under Just-In-Time Policy.

Item 5a. Animal Welfare Assurance

If the applicant organization has a current approved Animal Welfare Assurance on file with the Office of Laboratory Animal Welfare (OLAW), enter the Assurance number of the applicant organization in Item 5a. To determine whether the organization holds an Animal Welfare Assurance, contact the IACUC or see http://grants.nih.gov/grants/olaw/olaw.htm#assur.

Enter “None” in Item 5a if the applicant organization does not have an Animal Welfare Assurance on file with OLAW. **Do not enter the Animal Welfare Assurance number of any Project/Performance Site or collaborating institution.** The signature on the Face Page constitutes declaration that the applicant organization will comply with PHS Policy on Humane Care and Use of Laboratory Animals by submitting an Animal Welfare Assurance when requested by OLAW and providing verification of IACUC approval when requested by the PHS awarding component.

Item 6. Dates of Proposed Period of Support

Request no more than 5 years of support, unless specifically authorized in the FOA. Note that some programs specify fewer years.

New application. Consult the schedule at http://grants.nih.gov/grants/dates.htm for an appropriate beginning date. Refer to the FOA for beginning dates for PHS agencies other than NIH.

Renewal application. Choose a beginning date immediately following the termination date of the current period of support.

Revision application. **Submit a Revision application only for a period within the current period of the active grant.** At the time of submission, the Revision request must be within the time period of the original (parent) award period, and any extension must be done **before** submission. Make the ending date of the Revision’s first budget period coincide with the ending date of the budget period that is to be supplemented, regardless of the Revision’s beginning date. If requesting supplemental funds for the future years of a currently funded grant, make the future years’ budget periods coincide with those of the currently funded grant.

Budget Request

All amounts requested in Items 7 and 8 and on the budget pages must be in U.S. dollars.

Item 7. Costs Requested for Initial Budget Period

Item 7a. Direct Costs

From Form Page 4, enter the "Subtotal Direct Costs for Initial Budget Period."

Item 7b. Total Costs

Enter the sum of: 1) the "Total Direct Costs for Initial Budget Period" from Form Page 4 and 2) the Facilities and Administrative costs for the initial budget period, as calculated on the Checklist Form Page.

Note the "Total Direct Costs" used to calculate Item 7b includes any consortium F&A costs.

Item 8. Costs Requested for Proposed Period of Support

Item 8a. Direct Costs

From Form Page 5, enter the sum of "Subtotal Direct Costs" for all years.

Item 8b. Total Costs

Enter the sum of: 1) "Total Direct Costs for Entire Proposed Project Period" from Form Page 5; and, 2) the total Facilities and Administrative costs for all years calculated on the Checklist Form Page.

Note the "Total Direct Costs" used to calculate Item 8b includes any consortium F&A costs.

Item 9. Applicant Organization

Name the one organization that will be legally and financially responsible for the conduct of activities supported by the award.

Item 10. Type of Organization

Check the appropriate box. See definitions of Applicant Organization Types definitions in Part III, 3.

Item 11. Entity Identification Number, DUNS Number, Congressional District

Entity Identification Number. Enter the 12-digit Entity Identification Number (EIN) assigned to the applicant organization by the Department of Health and Human Services Payment Management System for payment and accounting purposes. This number is an expansion of the 9-digit EIN assigned by the IRS. If the institution has not yet been assigned a number, enter either (1) the organization's Internal Revenue Service employer identification number (nine digits) or (2) the words "Applied for" to indicate that the organization does not have an EIN but has applied to the local office of the IRS for one. **Do not enter the PD/PI's social security number**; it is not appropriate for this item.

Data Universal Numbering System (DUNS) number. Enter the DUNS number. Applicant organizations must provide a DUNS number when applying for Federal grants or cooperative agreements. The DUNS, a Universal Identifier number, is a nine-digit number assigned by Dun and Bradstreet Information Services. An authorized organizational official should be consulted to determine the appropriate number to enter. If the organization does not have a DUNS number, an authorized organizational official should complete the electronic 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.

Congressional District. Enter the number of the Congressional District of the applicant organization. To locate the appropriate district see http://congress.org/congressorg/dbq/officials/?lvl=L.

Item 12. Administrative Official to be Notified if Award is Made

Name the applicant organization administrative official to be notified if an award is made. Provide a complete address for postal delivery and the telephone, fax, and e-mail address for the administrative official.

Item 13. Official Signing for Applicant Organization

Name an individual authorized to act for the applicant organization and to assume the obligations imposed by the Federal laws, requirements, and conditions for a grant or grant application, including the applicable Federal regulations. Provide a complete address for postal delivery and the telephone, fax, and e-mail address for the signing official.

Item 14. Applicant Organization Certification and Acceptance

An original signature, in ink, is required. Only an institutional official with formal designated or delegated authority to sign on behalf of the organization may sign the form. The signature must be dated. *In signing the application Face Page, the Authorized Organizational Representative of the applicant organization certifies that the applicant organization will comply with all applicable policies, assurances and/or certifications referenced in the application.*

The applicant organization is responsible for verifying its eligibility and the accuracy, validity, and conformity with the most current institutional guidelines of all the administrative, fiscal, and scientific information in the application, including the Facilities and Administrative rate. Deliberate withholding, falsification, or misrepresentation of information could result in administrative actions, such as withdrawal of an application, suspension and/or termination of an award, debarment of individuals, as well as possible criminal penalties. The signer further certifies that the applicant organization will be accountable both for the appropriate use of any funds awarded and for the performance of the grant-supported project or activities resulting from this application. The grantee institution may be liable for the reimbursement of funds associated with any inappropriate or fraudulent conduct of the project activity.

Assurances and Certifications

The Assurances and Certifications listed below are explained in Part III: Policies, Assurances, Definitions, and Other Information. 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.

The policies, assurances and certifications listed below may or may not be applicable to the project, program, or type of applicant organization. If unable to certify compliance, provide an explanation and place it after the Checklist Form Page (5.6).

Human Subjects Research

Research on Transplantation of Human Fetal Tissue

Research Using Human Embryonic Stem Cells

Women and Minority Inclusion Policy

Inclusion of Children Policy

ClinicalTrials.gov Requirements

Vertebrate Animals

Debarment and Suspension

Drug-Free Workplace

Lobbying

Non-Delinquency on Federal Debt

Research Misconduct

Civil Rights

Handicapped Individuals

Sex Discrimination

Age Discrimination

Recombinant DNA, including Human Gene Transfer Research

Financial Conflict of Interest

Smoke-Free Workplace

Prohibited Research

Select Agent Research

Program Director/Principal Investigator(s) Assurance

Impact of Grant Activities on the Environment and Historic Properties

Institutions Receiving Awards for Training of Graduate Students for Doctoral Degrees

4.2 Description, Project/Performance Sites, Senior/key Personnel, Other Significant Contributors, and Human Embryonic Stem Cells

FORM PAGE 2 and 2-continued

Do NOT insert additional pages between Form Page 1 and Form Page 2.

4.2.1 Description: Project Summary and Relevance

The first and major component of the Description is a **Project Summary**. It is meant to serve as a succinct and accurate description of the proposed work when separated from the application. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project (i.e., relevance to the mission of the agency). Describe concisely the research design and methods for achieving the stated goals. This section should be informative to other persons working in the same or related fields and insofar as possible understandable to a scientifically or technically literate reader. Avoid describing past accomplishments and the use of the first person.

The second component of the Description is **Relevance**. Using no more than two or three sentences, describe the relevance of this research to public health. In this section, be succinct and use plain language that can be understood by a general, lay audience.

DO NOT EXCEED THE SPACE PROVIDED.

Use text only (no figures or other information not in standard text.) Do not include proprietary, confidential information or trade secrets in the description section. If the application is funded, the project description will be entered into an NIH database and will become public information.

4.2.2 Project/Performance Site(s)

Indicate where the work described in the Research Plan will be conducted. If there are more than two Project/Performance Sites, use the Project/Performance Site Format Page to list all the sites, including Department of Veterans Affairs (VA) facilities and foreign sites. Provide an explanation on the Resources Format Page of the application, and state whether a consortium/contractual arrangement is involved with one or more collaborating organizations for the conduct of a portion of the work described in the Research Plan. One of the sites indicated must be the applicant organization or be identified as off-site in accordance with the conditions of the applicant organization's negotiated Facilities and Administrative (F&A) agreement. This information must agree with the F&A information on the Checklist Form Page of the application.

If a Project/Performance Site is engaged in research involving human subjects, the applicant organization is responsible for ensuring that the Project/Performance Site operates under an appropriate Federal Wide Assurance for the protection of human subjects and complies with 45 CFR Part 46 and other NIH human subject related policies described in the PHS 398 and GPS.

For research involving live vertebrate animals, the applicant organization must ensure that all Project/Performance Sites hold OLAW-approved Assurances. If the applicant organization does not have an animal program or facilities and the animal work will be conducted at an institution with an Assurance, the applicant must obtain an Assurance from OLAW prior to an award.

4.2.3 Senior/key Personnel

In addition to the PD/PI, Senior/key Personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not salaries are requested.

Typically, these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level should be included 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 same definition.**

Senior/key Personnel must devote measurable effort (described in person months) to the project, whether or not salaries are requested. "Effort of zero person months" or "as needed" are not acceptable levels of involvement for those designated as Senior/key Personnel.

Start with the PD/PI(s). List the PD/PI's last name first. When multiple PIs are proposed, list the contact PI first, then all additional PIs in alphabetical order. Then list all other Senior/key Personnel in alphabetical order, last name first. For each individual provide name, eRA Commons User Name (if known), organization name (their institutional affiliation), and role on the project. Under role on the project, indicate how the individual will function on the proposed project. *Use additional consecutively numbered pages as necessary.*

4.2.4 Other Significant Contributors

This category identifies 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 "effort of zero person months" or "as needed." Individuals with measurable effort may **not** be listed as Other Significant Contributors (OSCs). Consultants should be included if they meet this definition.

A biosketch, including Research Support information, will be required for Senior/key Personnel and OSCs, as this highlights their relevant accomplishments. Reviewers use these pages to address the "investigator(s)" review criterion (see Research Project Evaluation Criteria in Section 6. The Peer Review Process).

However, if an award is to be made, Other Support information will not be required or accepted for OSCs since considerations of overlap do not apply to these individuals.

Should the level of involvement for an individual listed as an OSC increase to measurable effort, he/she must be redesignated as Senior/key Personnel. This change must be made before any compensation is charged to the project.

4.2.5 Human Embryonic Stem Cells

If the proposed project involves human embryonic stem cells, in this section list the registration number of the specific cell line(s) from the stem cell registry found at: http://stemcells.nih.gov/research/registry/eligibilityCriteria.asp. Use continuation pages as needed. If a specific line cannot be referenced at the time of application submission, include a statement that one from the registry will be used.

4.3 Research Grant Table of Contents

FORM PAGE 3

Provide the page number for each category listed on the Table of Contents. Place page numbers at the bottom of each page, and consecutively number pages throughout the application. **Do not include unnumbered pages, and do not use suffixes, such as 5a, 5b.**

4.4 Budget Instructions

FORM PAGE 4

DETAILED BUDGET FOR INITIAL BUDGET PERIOD

Each item listed on Form Page 4 must be clearly justified on Form Page 5. List only the direct costs requested in this application. Do not include any items that are treated by the applicant organization as Facilities and Administrative (F&A) costs according to a Federal rate negotiation agreement, except for those F&A costs included in consortium/contractual costs. Applications from foreign organizations must request budgets in U.S. dollars. Foreign organizations may not include any charge-back of customs and import fees, such as consular fees, customs surtax, value-added taxes (VAT) and other related charges.

Note: If you are requesting a budget of $500,000 direct costs or more for any year, you must obtain prior approval from Institute/Center staff. This limit is exclusive of any consortium F&A costs. If the subtotal Direct Costs on Form Page 5 equals or exceeds $500,000 in any year, prior approval is required. (See Policy on the Acceptance for Review of Unsolicited Applications That Request $500,000 or More in Direct Costs**.)** The following items pertain individually to the completion of Form Page 4 (Detailed Budget for Initial Budget Period – Direct Costs Only).

Personnel

Name. Starting with the PD/PI(s), list the names of all applicant organization employees who are involved on the project during the initial budget period, regardless of whether a salary is requested. Include all collaborating investigators, individuals in training, and support staff.

Role on Project. Identify the role of each individual listed on the project. Describe their specific functions under Justification on Form Page 5. Provide budget narrative for ALL personnel by position,

role, and level of effort using person months (calendar, academic and/or summer). This includes any "to-be-appointed" positions.

Months Devoted to Project. Enter the number of months devoted to the project. Three columns are provided depending on the type of appointment being reflected: academic, calendar, and/or summer months. Individuals may have consecutive appointments within a calendar year, for example for an academic period and a summer period. In this case, each appointment should be identified separately using the corresponding column.

If effort does not change throughout the year, use only the calendar months column. If effort varies between academic and summer months, leave the calendar months column blank and use only the academic and summer months columns. In cases where no contractual appointment exists with the applicant organization and salary is requested, enter the number of months for the requested period.

Institutional Base Salary. An applicant organization may choose to leave this column blank. However, PHS staff will require this information prior to award. See Definitions in Part III.3.

Salary Requested. Regardless of the number of months being devoted to the project, indicate only the amount of salary being requested for this budget period for each individual listed.

Some PHS grant programs are currently subject to a legislatively imposed salary limitation. Any adjustment for salary limits will be made at the time of award. For guidance on current salary limits see the *Salary Cap Summary* on the NIH grants Web site or contact the organization's office of sponsored programs.

NIH grants also limit the compensation for graduate students. Compensation includes salary or wages, fringe benefits and tuition remission. While actual institutional-based compensation should be requested and justified, this may be adjusted at the time of the award. For more guidance on this policy, see: http://grants.nih.gov/grants/ guide/notice-files/NOT-OD-02-017.html.

Fringe Benefits. Fringe benefits may be requested in accordance with institutional guidelines for each position, provided the costs are treated consistently by the applicant organization as a direct cost to all sponsors.

Totals. Calculate the totals for each position and enter the subtotals in each column where indicated.

The applicant organization and its consortium/contractor(s) may omit salaries and fringe benefits for individuals from copies of the application that are available to non-Federal reviewers. In such cases, replace the numbers with asterisks. You must show the subtotals. Provide one copy, for use only by PHS staff, with the asterisks replaced by the salaries and fringe benefits.

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 components.

Consultant Costs

Whether or not costs are involved, provide the names and organizational affiliations of all consultants, other than those involved in consortium/contractual arrangements. Include consultant physicians in connection with patient care and persons who are confirmed to serve on external monitoring or advisory committees. Describe the services to be performed on Form Page 5 under "Justification." Include the number of days of anticipated consultation, the expected rate of compensation, travel, per diem, and other related costs.

Equipment

List each item of equipment with amount requested separately and justify each purchase on Form Page 5.

Supplies

Itemize supplies in separate categories, such as glassware, chemicals, radioisotopes, etc. Categories in amounts less than $1,000 do not have to be itemized. If animals are to be purchased, state the species and the number to be used.

Travel

Itemize travel requests and justify on Form Page 5. Provide the purpose and destination of each trip and the number of individuals for whom funds are requested.

Patient Care Costs

If inpatient and/or outpatient costs are requested for research with human subjects, provide the names of any hospitals and/or clinics and the amounts requested for each on Form Page 5.

State whether each hospital or clinic has a currently effective DHHS-negotiated research patient care rate agreement and, if not, what basis is used for calculating costs. If an applicant does not have a DHHS-negotiated rate, the PHS awarding component can approve a provisional rate. Indicate, in detail, the basis for estimating costs in this category, including the number of patient days, estimated cost per day, and cost per test or treatment. If both inpatient and outpatient costs are requested, provide information for each separately. If multiple sites are to be used, provide detailed information by site.

Include information regarding projected patient accrual for the project/budget periods and relate this information to the budget request for patient care costs. If patient accrual is anticipated to be lower at the start or during the course of the project, plan budget(s) accordingly.

Provide specific information regarding anticipated sources of Other Support for patient care costs, e.g., third party recovery or pharmaceutical companies. Include any potential or expected utilization of General Clinical Research Centers/Clinical Translation Science Awards.

Alterations and Renovations

Itemize by category and justify on Form Page 5 the costs of essential alterations and renovations including repairs, painting, removal or installation of partitions, shielding, or air conditioning. Where applicable, provide the square footage and costs. Note, costs for any Alterations and Renovations (A&R) were previously unallowable from foreign institutions, international organizations and domestic applications with foreign subawards. However an HHS policy change now allows for minor A&R (<$500,000) on these applications. When requesting minor A&R costs under this policy, provide detailed information on the planned A&R in the budget justification.

Other Expenses

Itemize any other expenses by category and unit cost. These might include animal maintenance (unit care costs and number of care days), patient travel, patient participation incentives, donor fees, publication costs, computer charges, rentals and leases, equipment maintenance, service contracts, and tuition remission when budgeted separately from salary/fringe benefits. **Justify costs on Form Page 5.**

Consortium/Contractual Costs

Each participating consortium/contractual organization must submit a separate detailed budget for both the initial budget period (Form Page 4) and the entire proposed project period (Form Page 5).

Consortium arrangements may involve personnel costs, supplies, and other allowable costs, including Facilities and Administrative (F&A) costs. Contractual costs for support services, such as the laboratory testing of biological materials, clinical services, or data processing, are occasionally sufficiently high to warrant a similar categorical breakdown of costs.

For each budget from a participating consortium/contractual organization, leave the "Consortium/Contractual Direct Costs" category blank and use the "Subtotal Direct Costs" category to total the consortium direct costs. When F&A costs are requested by a consortium organization, enter those costs in the "Consortium/Contractual F&A Costs" category for each supplementary budget. Provide the F&A cost base and rate information in the budget justification section. The "Total Direct Costs for Initial Budget Period" category can be used for the consortium/contractual Total Costs (Direct Costs plus F&A).

For the applicant organization budget, list the sum of all consortium/contractual costs (direct and F&A). Insert additional budget page(s) after Form Page 5, numbering them sequentially. (Do not use 5a, 5b, 5c, etc.)

Budget Totals for Applicant Organization

For Face Page Item 7a, use the “Subtotal Direct Costs for Initial Budget Period” on Form Page 4.

For Face Page Item 7b, add together the “Total Direct Costs for Initial Budget Period” from Form Page 4 and the F&A costs calculated for the initial budget period on the Checklist Form Page.

For Face Page Item 8a, total the “Subtotal Direct Costs” for all years on Form Page 5 (see 4.5 below).

For Face Page Item 8b, add together the “Total Direct Costs for Entire Proposed Project Period” on Form Page 5 and the Total F&A costs for all years calculated on the Checklist Form Page.

Revision Application

For a Revision application, show only those items for which additional funds are requested. If the initial budget period of the Revision application is less than 12 months, prorate the personnel costs and other appropriate items of the detailed budget.

4.5 Budget for Entire Proposed Period of Support

FORM PAGE 5

In the first column enter the budget category totals of the initial budget period costs from Form Page 4.

Enter the totals under each budget category for all additional years of support requested. Identify with an asterisk (*), and justify any significant increases or decreases from the initial year budget. Also, justify budgets with more than a standard escalation from the initial to the future year(s) of support.

Justification for Foreign Application or Component

If the applicant organization is a foreign institution, or if the project includes a foreign component, provide a justification on Form Page 5. Describe special opportunities for furthering research programs through the use of unusual talents, resources, populations, or environmental characteristics that augment existing U.S. resources. Indicate whether similar research is being done in the United States. For a definition of foreign component, see Definitions in Part III.3.

4.6 Biographical Sketch

BIOGRAPHICAL SKETCH FORMAT PAGE

Follow the instructions on the Biographical Sketch Format Page. This section must contain the biographical sketches of all individuals listed as **Senior/key Personnel and Other Significant Contributors**, following the order as listed on Form Page 2.

All individuals who have the PD/PI role **must** be registered in the eRA Commons, and **must** include the assigned Commons User Name. This information is required, and is equivalent to the "Credential, e.g., agency login" in the federal-wide SF 424 (R&R) Senior/Key Person Profile. For information on the eRA Commons, see https://commons.era.nih.gov/commons/index.jsp.

Use the sample format on the Biographical Sketch Format Page to prepare this section for **all** grant applications. The Biographical Sketch may not exceed 4 pages. This 4-page limit includes the table at the top of the first page. (See sample of a completed Biographical Sketch: http://grants.nih.gov/grants/funding/phs398/phs398.html#biosample.)

Complete the educational block at the top of the format page beginning with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training, separately referencing residency training when applicable. For each entry provide the name and location of the institution, the degree received (if applicable) the month and year the degree was received; and the field of study. For residency entries, the field of study section should reflect the area of residency.

Following the educational block, complete sections A, B, C and D:

A. Personal statement. Briefly describe why your experience and qualifications make you particularly well-suited for your role (e.g., PD/PI, mentor) in the project that is the subject of the application.

B. Positions and Honors. List in chronological order previous positions, concluding with the present position. List any honors. Include present membership on any Federal Government public advisory committee.

C. Peer-reviewed publications or manuscripts in press. NIH encourages applicants to limit the list of selected peer-reviewed publications or manuscripts in press to no more than 15. Do not include manuscripts submitted or in preparation. The individual may choose to include selected publications based on recency, importance to the field, and/or relevance to the proposed research. When citing articles that fall under the Public Access Policy, were authored or co-authored by the applicant and arose from NIH support, provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the PubMed Central (PMC) reference number (e.g., PMCID234567) for each article. If the PMCID is not yet available because the Journal submits articles directly to PMC on behalf of their authors, indicate "PMC Journal - In Process." A list of these Journals is posted at: http://publicaccess.nih.gov/submit_process_journals.htm. Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PMCID numbers along with the full reference (note that copies of publicly available publications are not acceptable as appendix material.)

D. Research Support. List both selected ongoing and completed research projects for the past three years (Federal or non-Federally-supported). *Begin with the projects that are most relevant to the research proposed in the application.* Briefly indicate the overall goals of the projects and responsibilities of the key person identified on the Biographical Sketch. Do not include number of person months or direct costs.

Do not confuse "Research Support" with "Other Support." Though they sound similar, these parts of the application 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 qualifications 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 (see Part I, 4.6.1). 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 beyond that required in the biographical sketch should NOT be submitted with the application.

4.6.1 Other Support Information

OTHER SUPPORT FORMAT PAGE

Do not submit unless requested by the NIH Institute/Center (IC).

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

The following instructions should be followed in completing the information:

- 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/subcontract 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.

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 subcontract.

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.

Special Instructions for Individuals with Multiple Research Appointments (e.g., dual university/Department of Veterans Affairs appointments)

When an individual holds multiple appointments involving support for research activities, information from each appointment must be included separately in the Other Support documentation. The support from each funding source should be clearly and separately delineated so that the separate appointments can be considered independently when determining any potential overlap.

List each appointment separately and include enough information on the type of appointment; (e.g., full time academic or 6/8 VA) so that an assessment of an individual's commitment can be made. Within each appointment, include appropriate sources of research support providing the standard detailed information cited above.

Note that when an individual has multiple appointments it is possible that the combined effort can result in excess of 12 calendar months (not from any one institution, but a combination of multiple appointments). In all cases, an individual's combined total professional effort must meet a test of reasonableness.

4.7 Resources

RESOURCES FORMAT PAGE

This information is used to assess the capability of the organizational resources available to perform the effort proposed.

- Identify the facilities to be used (laboratory, clinical, animal, computer, office, other). If appropriate, indicate their capacities, pertinent capabilities, relative proximity and extent of availability to the project. Describe only those resources that are **directly applicable** to the proposed work. Provide any information describing the Other Resources available to the project (e.g., machine shop, electronic shop) and the extent to which they would be available to the project.
- Describe how the scientific environment in which the research will be done contributes to the probability of success (e.g., institutional support, physical resources, and intellectual rapport). In describing the scientific environment in which the work will be done, discuss ways in which the proposed studies will benefit from unique features of the scientific environment or subject populations or will employ useful collaborative arrangements.
- For Early Stage Investigators, describe institutional investment in the success of the investigator, e.g., resources for classes, travel, training; collegial support such as career enrichment programs, assistance and guidance in the supervision of trainees involved with the ESIs project, and availability of organized peer groups; logistical support such as administrative management and oversight and best practices training; and financial support such as protected time for research with salary support.
- If there are multiple performance sites, describe the resources available at each site.
- Describe any special facilities used for working with biohazards or other potentially dangerous substances. Note: Information about Select Agents must be described in the Research Plan, 5.5.11 (Select Agent Research).

4.8 All Personnel Report

ALL PERSONNEL REPORT FORMAT PAGE - Renewal Applications Only

Use **only** when requested by the awarding component.

Always list the PD/PI(s). In addition, **list all other personnel** (salaried and unsalaried) **for the current budget period** at the applicant organization or elsewhere, who participated in the project during the current budget period for at least one person month or more, regardless of the source of compensation. A person month equals approximately 160 hours or 8.3% of annualized effort. Include the Commons ID (when applicable) names of individuals, all degrees, the last four digits of the Social Security number, role on project, date of birth (MM/YY), and number of person months devoted to the project (indicate academic, calendar, and/or summer).

When requesting the last four digits of the Social Security numbers from personnel, explain that provision of the Social Security number is voluntary, and the information will be used only for program management purposes. The Commons ID is required for all PD/PIs and all individuals with a postdoctoral role; it is optional for all other personnel.

Use the following categories for describing Role on Project:

- PD/PI
- Co-Investigator
- Faculty Collaborator
- Staff scientist (doctoral level)
- Postdoctoral Scholar, Fellow, or Other Postdoctoral Position
- Graduate Research Assistant
- Undergraduate Research Assistant
- Research Assistant/Coordinator
- Technician
- Consultant
- Other (please specify)

If personnel are supported by a Reentry or Diversity Supplement or American Recovery and Reinvestment Act (ARRA) funding, please indicate such after the Role on Project, using the following abbreviations:

- RS - Reentry Supplement
- DS - Diversity Supplement
- AF - General ARRA Supplement
- ASE - ARRA Summer Experience funding

Individuals designated as Other Significant Contributors, e.g. those that may contribute to the scientific development or execution of the project, but are not committing any specified measurable effort to the project, should **not** be included in this report unless their involvement has changed so that they are now participating in the project during the current budget period for at least one person month or more.

5. Preparing the Research Plan, the Checklist, and the Appendix

5.1 (Reserved)

5.2 (Reserved)

5.3 (Reserved)

5.4 Research Plan Format and Notice of Proprietary Information

5.4.1 Research Plan Format

No Specific Form Page - Use CONTINUATION PAGE

The Research Plan consists of items 1-15 in Section 5.5 below, as applicable. It should be self-contained and include sufficient information to evaluate the project, independent of any other document (e.g., previous application). Be specific and informative, and avoid redundancies. For grant writing tips, see http://grants.nih.gov/grants/grant_tips.htm. Carefully follow all instructions.

Page Limits

All applicants must follow the page limits described in 2.6, unless the FOA specifies otherwise. All tables, graphs, figures, diagrams, and charts must be included within the Research Strategy page limit. If PAs or RFAs contain specific page limits, those instructions always supersede these PHS 398 instructions.

Use of URLs

Unless otherwise specified in a solicitation, Internet website addresses (URLs) may not be used to provide information necessary to the review because reviewers are not obligated to view the Internet sites. Moreover, reviewers are cautioned that they should not directly access an Internet site (except to review publications cited in the Biographical Sketch or Progress Report Publication List) as it could compromise their anonymity.

Other Materials

Do not include photographs or other materials that are not printed directly on the application page in the body of the application. Pictures or other materials glued or taped into the application pages are incompatible with the duplication/scanning process.

PDF images of material such as electron micrographs or gels may be included in the Appendix; however, a photocopy of each must also be included within the page limits of the Research Strategy (see Section 5.7).

5.4.2 Notice of 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, or information that is commercial or financial, or information that is confidential or privileged, identify the pages in the application that contain this information by marking those paragraphs or lines with an asterisk (*) at the beginning of the paragraph. Indicate at the beginning of the Research Plan which pages contain asterisks and a note stating: *"The following*

sections marked with an asterisk contain proprietary/privileged information that [name of applicant] requests not be released to persons outside the Government, except for purposes of review and evaluation."

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 as a result 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.

5.5 Content of Research Plan

The Research Plan consists of the following items (5.5.1 – 5.5.15), as applicable. Begin each section of the Research Plan with a section header (e.g., Introduction, Specific Aims, Research Strategy, etc.).

The Research Strategy, Section 5.5.3, is composed of three distinct sections – Significance, Innovation, and Approach. Note the Approach section also includes Preliminary Studies for new applications and a Progress Report for renewal and revision applications.

Applicants must follow the table of page limits in Part I, 2.6, unless specified otherwise in the FOA. If the activity code is not listed in the table of page limits, follow the page limits required in the FOA. All page limits include all tables and figures.

1. Introduction to Application (Resubmission or Revision Applications only)
2. Specific Aims
3. Research Strategy (Significance, Innovation and Approach)
4. Inclusion Enrollment Report (Renewal or Revision Applications only)
5. Bibliography and References Cited/Progress Report Publication List
6. Protection of Human Subjects
7. Inclusion of Women and Minorities
8. Targeted/Planned Enrollment Table
9. Inclusion of Children
10. Vertebrate Animals
11. Select Agent Research
12. Multiple PD/PI Leadership Plan
13. Consortium/Contractual Arrangements
14. Letters of Support (e.g., Consultants)
15. Resource Sharing Plan(s)

5.5.1 Introduction (Resubmission or Revision Applications only)

See specific instructions in 2.7 Resubmission Applications and 2.8 Revision Applications on the content of the Introduction. First time (new) applications should not include an Introduction unless specified in the FOA.

The Introduction is limited to one page unless specified otherwise in the FOA.

5.5.2 Specific Aims

State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will exert on the research field(s) involved.

List succinctly the specific objectives of the research proposed, e.g., to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology.

Specific Aims are limited to one page.

5.5.3 Research Strategy

Organize the Research Strategy in the specified order and using the instructions provided below. Start each section with the appropriate section heading—Significance, Innovation, Approach. Cite published experimental details in the Research Strategy section and provide the full reference in the Bibliography and References Cited section (item 5.5.5).

Follow the page limits for the Research Strategy in the Table of Page Limits, unless specified otherwise in the FOA.

(a) Significance

- Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses.
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

(b) Innovation

- Explain how the application challenges and seeks to shift current research or clinical practice paradigms.
- Describe any novel theoretical concepts, approaches or methodologies, instrumentation or intervention(s) to be developed or used, and any advantage over existing methodologies, instrumentation or intervention(s).
- Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation or interventions.

(c) Approach

- Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project. Unless addressed separately in Item 5.5.15, include how the data will be collected, analyzed, and interpreted as well as any resource sharing plans as appropriate.
- Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.
- If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work.
- Point out any procedures, situations, or materials that may be hazardous to personnel and precautions to be exercised. A full discussion on the use of Select Agents should appear in 5.5.11 below.

As applicable, also include the following information as part of the Research Strategy, keeping within the three sections listed above: Significance, Innovation, and Approach.

- ***Preliminary Studies for New Applications.*** For new applications, include information on Preliminary Studies as part of the Approach section. Discuss the PD/PI's preliminary studies, data, and/or experience pertinent to this application. Except for Exploratory/Development Grants (R21/R33), Small Research Grants (R03), Academic Research Enhancement Award (AREA) Grants (R15), and Phase I Small Business Research Grants (R41/R43), preliminary data can be an essential part of a research grant application and help to establish the likelihood of success of the proposed project. Early Stage Investigators should include preliminary data. (However, for R01 applications, reviewers will be instructed to place less emphasis on the preliminary data in applications from Early Stage Investigators than on the preliminary data in applications from more established investigators.)
- ***Progress Report for Renewal and Revision Applications.*** For renewal/revision applications, provide a Progress Report as part of the Approach section. Provide the beginning and ending dates for the period covered since the last competitive review. Summarize the specific aims of the previous project period and the importance of the findings, and emphasize the progress made toward their achievement. Explain any significant changes to the specific aims and any new directions including changes resulting from significant budget reductions. A list of publications, manuscripts accepted for publication, patents, and other printed materials should be included in 5.5.5; do not include that information here.

5.5.4 Inclusion Enrollment Report (Renewal or Revision Applications only)

If the Renewal or Revision application involves clinical research, then you must report on the enrollment of research subjects and their distribution by ethnicity/race and sex/gender using the Inclusion Enrollment Report for each protocol.

5.5.5 Bibliography and References Cited/Progress Report Publication List

When citing articles in (a) or (b) below that fall under the Public Access Policy, were authored or co-authored by the applicant and arose from NIH support, provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the PubMed Central (PMC) reference number (e.g., PMCID234567) for each article. If the PMCID is not yet available because the Journal submits articles directly to PMC on behalf of their authors, indicate "PMC Journal - In Process." A list of these Journals is posted at: http://publicaccess.nih.gov/submit_process_journals.htm. Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PMCID numbers along with the full reference (note that copies of these publications are not accepted as appendix material, see Section 5.7).

(a) Bibliography and References Cited - Provide a bibliography of any references cited in the Research Plan. Each reference must include names of all authors (in the same sequence in which they appear in the publication), the article and journal title, book title, volume number, page numbers, and year of publication. Include only bibliographic citations. Follow scholarly practices in providing citations for source materials relied upon in preparing any section of the application.

The references should be limited to relevant and current literature. While there is not a page limitation, it is important to be concise and to select only those literature references pertinent to the proposed research.

(b) Progress Report Publication List - For Renewal applications list the titles and complete references to all appropriate publications, manuscripts accepted for publication, patents, and other printed materials that have resulted from the project since it was last reviewed competitively.

5.5.6 Protection of Human Subjects

Refer to Part II of the PHS 398: Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan if the proposed research will involve human subjects.

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

5.5.7 Inclusion of Women and Minorities

To determine if Inclusion of Women and Minorities applies to the application, see Part II Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan, Sections 4.2 and 5.6.

5.5.8 Targeted/Planned Enrollment Table

If this application involves the Inclusion of Women and Minorities, complete the Targeted/Planned Enrollment Table for each protocol; see Part II Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan, Section 4.3.

5.5.9 Inclusion of Children

To determine if Inclusion of Children applies to the application, see Part II Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan, Sections 4.4 and 5.7.

5.5.10 Vertebrate Animals

If vertebrate animals are involved in the project, address each of the five points below.

If all or part of the proposed research involving vertebrate animals will take place at alternate sites (such as project/performance or collaborating site(s)), identify those sites and describe the activities at those locations.

Although no specific page limitation applies to this section of the application, be succinct. Failure to address the following five points will result in the application being designated as incomplete and will be grounds for the PHS to defer the application from the peer review round. Alternatively, the application's impact/priority score may be negatively affected.

The five points are as follows:

1. Provide a detailed description of the proposed use of the animals for the work outlined in the Research Strategy section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.
2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.
3. Provide information on the veterinary care of the animals involved.
4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.

5. Describe any method of euthanasia to be used and the reason(s) for its selection. State whether this method is consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. If not, include a scientific justification for not following the recommendations.

If the involvement of animals is indefinite, provide an explanation and indicate when it is anticipated that animals will be used. If an award is made, prior to the involvement of animals the grantee must submit to the NIH awarding office detailed information as required in 1-5 above and verification of IACUC approval. If the grantee does not have an Animal Welfare Assurance then an appropriate Assurance will be required (see Part III, 2.2).

Do not use the vertebrate animal section to circumvent the page limits of the Research Strategy.

5.5.11 Select Agent Research

Select Agents are hazardous biological agents and toxins that have been identified by DHHS or USDA as having the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal and plant products. CDC maintains a list of these agents; see http://www.cdc.gov/od/sap/docs/salist.pdf.

If the activities proposed in the application involve only the use of a strain(s) of Select Agents which has been excluded from the list of select agents and toxins as per 42 CFR 73.3, the Select Agent requirements do not apply. Use this section to identify the strain(s) of the Select Agent that will be used and note that it has been excluded from this list. The CDC maintains a list of exclusions at http://www.cdc.gov/od/sap/sap/exclusion.htm.

If the strain(s) is not currently excluded from the list of select agents and toxins but you have applied or intend to apply to DHHS for an exclusion from the list, use this section to indicate the status of the request or the intent to apply for an exclusion and provide a brief justification for the exclusion.

If any of the activities proposed in the application involve the use of Select Agents at any time during the proposed project period, either at the applicant organization or at any other Project/Performance Site, address the following three points for each site at which Select Agent research will take place. Although no specific page limitation applies to this section, be succinct.

1. Identify the Select Agent(s) to be used in the proposed research.
2. Provide the registration status of all entities* where Select Agent(s) will be used.
    - If the Project/Performance Site(s) is a foreign institution, provide the name(s) of the country or countries where Select Agent research will be performed.

    *An “entity” is defined in 42 CFR 73.1 as “any government agency (Federal, State, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity.”
3. Provide a description of all facilities where the Select Agent(s) will be used.
    - Describe the procedures that will be used to monitor possession, use and transfer of the Select Agent(s).
    - Describe plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).
    - Describe the biocontainment resources available at all performance sites.

If you are responding to a specific Funding Opportunity Announcement (e.g., PA or RFA), address any requirements specified by the FOA.

Reviewers will assess the information provided in this section, and any questions associated with Select Agent research will need to be addressed prior to award.

5.5.12 Multiple Project Director/Principal Investigator (PD/PI) Leadership Plan

For applications designating multiple PD/PIs, a leadership plan must be included. A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and the research project should be described, including communication plans, process for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PD/PIs, including responsibilities for human or live vertebrate animal subject studies as appropriate.

If budget allocation is planned, the distribution of resources to specific components of the project or the individual PD/PIs should be delineated in the Leadership Plan. In the event of an award, the requested allocations may be reflected in a footnote on the Notice of Award.

5.5.13 Consortium/Contractual Arrangements

Explain the programmatic, fiscal, and administrative arrangements to be made between the applicant organization and the consortium organization(s). For applications including multiple PD/PIs, this information may be included as part of the Leadership Plan above. If consortium/contractual activities represent a significant portion of the overall project, explain why the applicant organization, rather than the ultimate performer of the activities, should be the grantee.

The signature of the authorized organizational official on the Face Page signifies that the applicant and all proposed consortium participants understand and agree to the following statement: *The appropriate programmatic and administrative personnel of each organization involved in this grant application are aware of the agency's consortium agreement policy and are prepared to establish the necessary inter-organizational agreement(s) consistent with that policy.*

5.5.14 Letters of Support (e.g., Consultants)

Provide all appropriate letters of support, including any letters necessary to demonstrate the support of consortium participants and collaborators such as Senior/Key Personnel and Other Significant Contributors included in the grant application. Letters are not required for personnel (such as research assistants) not contributing in a substantive, measurable way to the scientific development or execution of the project. For consultants, letters should include rate/charge for consulting services. Do **not** place these letters in the Appendix. Consultant biographical sketches should be in the Biographical Sketch section.

5.5.15 Resource Sharing Plan(s)

NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. See Part III, 1.5 Sharing Research Resources.

(a) Data Sharing Plan: Investigators seeking $500,000 or more in direct costs (exclusive of consortium F&A) in any year are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible. Specific FOAs may require that all applications include this information regardless of the dollar level. Applicants are encouraged to read the specific opportunity carefully and 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. See Data-Sharing Policy or http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html.

(b) Sharing Model Organisms: Regardless of the amount requested, 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 organisms or state appropriate reasons why such sharing is restricted or not possible. See Sharing Model Organisms Policy, and NIH Guide NOT-OD-04-042.

(c) Genome-Wide Association Studies (GWAS): Regardless of the amount requested, applicants seeking funding for a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. GWAS is defined as any study of genetic variation across the entire genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight) or the presence or absence of a disease or condition. For further information see Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, NIH Guide NOT-OD-07-088, and http://grants.nih.gov/grants/gwas/.

5.6 Checklist

CHECKLIST FORM PAGE

Type of Application

Check all that apply.

Inventions and Patents (Renewal Applications Only)

If no inventions were conceived or reduced to practice during the course of work under this project, check “No.” The remaining parts of the item are then not applicable.

If any inventions were conceived or reduced to practice during the previous period of support, check “Yes.” Also indicate whether this information has been reported previously to the PHS or to the applicant organization official responsible for patent matters.

Note: NIH recipient organizations must promptly report inventions to the Extramural Inventions and Technology Resources Branch of the Office of Policy for Extramural Research Administration, OER, NIH, Bethesda, MD 20892-2750, (301) 435-1986. Invention reporting compliance according to regulations at 37 CFR 401.14 is described at http://www.iedison.gov. The grantee is encouraged to submit reports electronically using Interagency Edison (http://www.iedison.gov). See also “Inventions and Patents” in Part III, 1.6.

1. Program Income

If no program income is anticipated during the period(s) for which grant support is requested, so state.

If program income is anticipated, use the format provided. If the application is funded, the Notice of Award will provide specific instructions regarding the use of such income.

2. Assurances/Certifications

Each application to the PHS requires that the policies, assurances, and certifications provided in Part III and listed in Part 1, 4.1 under Item 14, be verified by the signature of the official signing for the applicant organization on the Face Page of the application.

3. Facilities and Administrative (F&A) Costs

Indicate the applicant organization’s most recent F&A cost rate established with the appropriate DHHS Regional Office, or, in the case of for-profit organizations, the rate established with the Division of Financial Advisory Services (DFAS), NIH. If the applicant organization does not have a current negotiated rate, it should develop a provisional rate for application purposes, and immediately upon notification that an award will be made, it should submit the provisional F&A cost rate proposal to the appropriation negotiation office. This proposal is to be based on the organization’s most recently completed fiscal year in accordance with the principles set forth in the pertinent DHHS guidance for

establishing indirect cost rates, and submitted to the appropriate DHHS Regional Office or the DFAS, NIH. If the applicant organization has a current negotiated rate with another Federal agency, the negotiated rate must be adjusted to treat any independent research and development (IR&D) costs in accordance with DHHS policy. F&A costs will NOT be paid on construction grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Institutional Training, including Ruth L. Kirschstein National Research Service Awards, and specialized grant applications.

Foreign institutions and international organizations (non-U.S. entities) may request funds for limited F&A costs (8 percent of modified total direct costs less equipment) to support the costs of compliance with DHHS and NIH requirements including, but not limited to, protection of human subjects, animal welfare, invention reporting, financial conflict of interest and research misconduct.

4. Disclosure Permission Statement

In the case this application does not result in an award, check “yes” to provide permission for the Government to disclose the title of the proposed project, and the name, address, telephone number and email address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment). Check “no” if you do not provide this permission. Your response will not affect any peer review or funding decisions.

5.7 Appendix

Do not use the appendix to circumvent the page limits of the Research Strategy. Graphs, diagrams, tables, and charts should be included in the body of the Research Strategy unless a PDF file is necessary to show detail. Not all activity codes allow publications to be included in the appendix. When publications are allowed, a limit of 3 publications, which are not publicly available, will be considered in the initial peer review (see below for further details and check the FOA for any specific instructions). A summary listing all of the items included in the appendix is encouraged, but not required. When including a summary, it should be the first file on the CD. Applications that do not follow the appendix requirements may be delayed in the review process.

Five identical CDs containing all appendix material must be submitted in the same package with the application. When preparing CDs:

- Use PDF format. Where possible, applicants should avoid creating PDF files from scanned documents. NIH recommends producing the documents electronically using text or word-processing software and then converting to PDF. Scanned documents are generally of poor quality and difficult to read.
- Label each disk with the PD/PI name and application title.
- If burning CD-ROM disks on a Mac, select the ISO 9660 format.
- Do not use compression techniques for the electronic files.
- Do not use password protection, encryption, digital signature and/or digital certification in the PDF files.

The following materials may be included in the appendix to New, Revision, Renewal and Resubmission applications (note, however, that some FOAs do not permit publications):

- Up to 3 publications of the following types. In each case include the entire document:
    - Manuscripts and/or abstracts accepted for publication but not yet published.
    - Published manuscripts and/or abstracts where a free, online, publicly available journal link is not available.

    - Patents directly relevant to the project.

  Do not include unpublished theses or abstracts/manuscripts submitted, but not yet accepted, for publication.

- Surveys, questionnaires, and other data collection instruments, clinical protocols, and informed consent documents.
- Color images of gels, micrographs, etc., provided that a photocopy (may be reduced in size) is also included within the page limit of the Research Strategy. No images may be included in the appendix that are not also represented within the Research Strategy.
- For materials that cannot be submitted on CD (e.g., medical devices, prototypes), applicants should contact the Scientific Review Officer for instructions following notification of assignment of the application to a SRG. Applicants are encouraged to be as concise as possible and submit only information essential for the review of the application.

Publications that are publicly accessible must not be included in the appendix. For such publications, the URL or PMC submission identification numbers along with the full reference should be included as appropriate in the Bibliography and References Cited/Progress Report Publication List section of the Research Plan, and/or in the Biographical Sketch.

6. The Peer Review Process

Overview

NIH policy is intended to ensure that applications for funding submitted to the NIH are evaluated on the basis of a process that is fair, equitable, timely, and conducted in a manner free of bias. The NIH dual peer review system is mandated by statute in accordance with section 492 of the Public Health Service Act and federal regulations governing "Scientific Peer Review of Research Grant Applications and Research and Development Contract Proposals" (42 CFR Part 52h).

The first level of review is carried out by a Scientific Review Group (SRG) composed primarily of non-federal scientists who have expertise in relevant scientific disciplines and current research areas. The second level of review is performed by Institute and Center (IC) National Advisory Councils or Boards. Councils composed of both scientific and lay members are chosen for their expertise, interest, or activity in matters related to health and disease. Only applications that are favorably recommended by both the SRG and the Advisory Council may be recommended for funding. Only the NIH Institute or Center may make actual funding decisions.

A detailed description of what happens to a research project grant application after it is received for peer review can be found at the following location: http://grants.nih.gov/grants/peer_review_process.htm. Additional information about charters and membership of SRGs, Councils, and Boards can be obtained from the appropriate agency. Information on CDC review procedures is located at http://www.cdc.gov/od/science/PHResearch/peerreview.htm.

Streamlining

The initial scientific peer review of most applications will also include a process in which only those applications deemed by the reviewers to have the highest scientific and technical merit, generally the better half of the applications under review, will be discussed at the SRG meeting, assigned an impact score, and receive a second level review. Applications in the lower half are reviewed by SRG members but they are not discussed or scored at the SRG meeting. This process allows the reviewers to focus their discussion on the most meritorious applications.

Before the review meeting, each reviewer and discussant assigned to an application will give a separate score for each of the five core review criteria and a preliminary impact score for that application (see below). The preliminary impact scores will be used to determine which applications will be discussed.

Scoring

SRG members are instructed to evaluate research applications by addressing the five core review criteria (see below) and additional review criteria as applicable for the application. However, Requests for Applications (RFAs) and other types of funding opportunities (e.g., construction grants and fellowship applications) may list different and/or additional review criteria and considerations.

For each application that is discussed, a final overall impact score will be given by each eligible committee member (without conflicts of interest) following the panel discussion. Each member's impact score will reflect his/her evaluation of the overall impact of the project in its entirety, rather than an arithmetic formula applied to the reviewer's scores given to each criterion. The final impact score for each discussed application will be determined by calculating the arithmetic average of all the eligible members' impact scores, and multiplying the average by 10.

As part of the initial merit review, and regardless of whether an application is discussed or not discussed (streamlined), all applicants will receive a written critique, called a Summary Statement, unless stated otherwise in the FOA. The Summary Statement represents a combination of the reviewers' written comments and scores for individual criteria. The Summary Statement for discussed applications includes the Scientific Review Officer's summary of the members' discussion during the SRG meeting; the final impact score; the recommendations of the SRG, including budget recommendations; and administrative notes of special considerations. For applications that are not discussed by the full committee, the scores of the assigned reviewers and discussants for the five core criteria will be reported individually on the Summary Statement. Final impact scores are not given for applications that are not discussed.

Research Project Evaluation Criteria

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

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

> ***Significance.*** Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?
>
> ***Investigator(s).*** Are the PD/PIs, collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?
>
> ***Innovation.*** Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or

interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Approach. Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed?

If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

Environment. Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Additional Review Criteria. As applicable for the project proposed, reviewers will consider the following additional items in the determination of scientific and technical merit, but will not give separate scores for these items.

Protections for Human Subjects. For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials.

Inclusion of Women, Minorities, and Children. When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children.

Vertebrate Animals. The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia.

Resubmission Applications. When reviewing a Resubmission application (formerly called an amended application), the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewal Applications. When reviewing a Renewal application (formerly called a competing continuation application), the committee will consider the progress made in the last funding period.

Revision Applications. When reviewing a Revision application (formerly called a competing supplement application), the committee will consider the appropriateness of the proposed

expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

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

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

Budget and Period Support. Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

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

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

Resource Sharing Plans. Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: 1) Data Sharing Plan (http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm); 2) Sharing Model Organisms (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html); and 3) Genome Wide Association Studies (GWAS) (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html).

Dual-Level Peer Review

The second level of review will usually be performed by the Advisory Council or Board of the potential awarding component (Institute, Center, or other unit). Council or Board recommendations are based not only on considerations of scientific merit, as judged by the SRGs, but also on the relevance of the proposed study to an Institute/Center's mission, programs and priorities.

PART II

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

1. Introduction

A Protection of Human Subjects section of the Research Plan is required for all applications submitted using the PHS 398 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 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 website: 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 Targeted/Planned Enrollment Table, and the Inclusion of Children (items 7, 8, and 9 of the Research Plan). 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 DHHS 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.

2. Scenarios

Scenario A. No Human Subjects Research

If no human subjects research is proposed in the application, you will have designated “No” in Item 4. on the PHS 398 face page. 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.

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 Item 4 on the PHS 398 face page. 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 DHHS 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 DHHS regulations (46.101(b)), “yes” should be designated in item 4 and in item 4a on the PHS 398 face page. In the section on Protection of Human Subjects in the Research Plan, 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 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 website http://www.hhs.gov/ohrp/ for guidance and further information.

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

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 website: 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 DHHS regulations (45 CFR Part 46.118), you will have designated “Yes” in Item 4. on the PHS 398 face page. In the section on Protection of Human Subjects in the Research Plan, 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 undergo an independent decision-making process (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 during the project period, you will have designated “Yes” in Item 4 on the PHS 398 face page, “No” in Item 4a on the PHS 398 face page, and “Yes” in Item 4c on the PHS 398 face page.

In the section on Protection of Human Subjects in the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets:

1) the requirements of the DHHS regulations to protect human subjects from research risks (45 CFR Part 46);
2) 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 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 Item 4 on the PHS 398 face page, "No" in Item 4a on the PHS 398 face page, and "Yes" in Item 4d on the PHS 398 face page. In the section on Protection of Human Subjects in the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets:

1) the requirements of the DHHS regulations to protect human subjects from research risks (45 CFR Part 46);
2) 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 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

In the application narrative, 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."

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.

The explanation could 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/humansubjects/guidance/cdebiol.htm).

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, create a section entitled "Protection of Human Subjects" and create a subheading for each of the following items.

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

Targeted/Planned Enrollment Table(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 DHHS 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, provide the required information for each of the following topics below:

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.

If the research will include a clinical trial, 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

Targeted/Planned Enrollment Table(s) - Section 4.3

Inclusion of Children - Section 4.4

*NOTE: If all the proposed research meets the criteria for Exemption 4, then the requirements for inclusion of women and minorities, targeted/planned enrollment table, 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 clinical research, the request for prior approval must also address the inclusion of women and minorities, the

inclusion of children, and provide completed targeted/planned enrollment tables 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.

In the application narrative, create a section entitled Protection of Human Subjects and a subheading for each of the following items. 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, 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

Targeted/Planned Enrollment Table(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, 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. 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

Inclusion of Women and Minorities - Section 4.2

Targeted/Planned Enrollment Table(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
Exempt:	No
Clinical Trial:	Yes

NIH-Defined Phase III Clinical Trial: Yes

Instructions and Required Information

In the application narrative, 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 following items. 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

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

Targeted/Planned Enrollment Table(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, create a section entitled “Protection of Human Subjects.” 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. DHHS 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, as well as the recruitment and 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 the potential risks to subjects (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 DHHS regulations, Subparts B-D must include additional protections. Refer to DHHS regulations, and OHRP guidance:
    - Additional Protections for Pregnant Women, Human Fetuses and Neonates: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartb
    - Additional Protections for Prisoners: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#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.htm#subpartd
- OHRP Subpart D Guidance: http://www.hhs.gov/ohrp/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 (biomedical and behavioral intervention studies) 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 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.

4.1.4 Importance of the Knowledge to be Gained

- Discuss the importance of the knowledge gained or 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, 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), the funding I/C, 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 websites 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:

a. PD/PI (required)

b. Institutional Review Board (IRB) (required)

c. Independent individual/safety officer

d. Designated medical monitor

e. Internal Committee or Board with explicit guidelines

f. 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.

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

For new and renewal (competing) applications that include applicable clinical trials which require registration and results reporting under FDAAA, provide the NCT number/s, Brief Title/s (protocol title intended for the lay public - see Definitions), and the identity (name, organization, and e-mail address required for internal administrative use only) of the responsible party (or parties) in the human subjects section of the Research Plan under a section heading entitled ClinicalTrials.gov. If a new applicable clinical trial is proposed, under the heading ClinicalTrials.gov, provide a clear statement in the human subjects section of the Research Plan that the application includes an applicable clinical trial which requires registration in 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 C.F.R. 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 Organizational Representative assures compliance with FDAAA.

Additional information can be found on the ClinicalTrials.gov website (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 limitation applies to this section of the application, be succinct. The NIH Policy on the Inclusion of Women and Minorities in Clinical Research is described and referenced in Section 5.6.

Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the inclusion of women and minorities in clinical research.

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

1. The targeted/planned distribution of subjects by sex/gender and racial/ethnic groups for each proposed study or protocol using the format in the Targeted/Planned Enrollment Table. (Instructions for completing this table are provided below in 4.3.) If using existing specimens and/or data without access to information on the distribution of women and minorities, so state and explain the impact on the goals of the research as part of the rationale that inclusion cannot be described (item 3 below). Alternatively, describe the gender and minority composition of the population base from whom the specimens and/or data will be obtained. Include the Targeted/Planned Enrollment Tables in this section.
2. A description of the subject selection criteria and rationale for selection of sex/gender and racial/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. A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group (see examples below).
4. A description of proposed outreach programs for recruiting sex/gender and racial/ethnic group members as subjects.

Below are examples of acceptable justifications for the exclusion of:

A. ***One gender:***

1. One gender is excluded from the study because:
   - inclusion of these individuals would be inappropriate with respect to their health;
   - the research question addressed is relevant to only one gender;
   - evidence from prior research strongly demonstrates no difference between genders; or
   - sufficient data already exist with regard to the outcome of comparable studies in the excluded gender, and duplication is not needed in this study.
2. One gender is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; 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).

3. Gender representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or data-sets with incomplete gender documentation are used), and this does not compromise the scientific objectives of the research.

B. ***Minority groups or subgroups:***

1. Some or all minority groups or subgroups are excluded from the study because:
   - inclusion of these individuals would be inappropriate with respect to their health;
   - the research question addressed is relevant to only one racial or ethnic group;
   - evidence from prior research strongly demonstrates no differences between racial or ethnic groups on the outcome variables;
   - a single minority group study is proposed to fill a research gap; or
   - sufficient data already exists with regard to the outcome of comparable studies in the excluded racial or ethnic groups and duplication is not needed in this study.
2. Some minority groups or subgroups are excluded or poorly represented because the geographical location of the study has only limited numbers of these minority groups who would be eligible for the study, and the investigator has satisfactorily addressed this issue in terms of:
   - the size of the study;
   - the relevant characteristics of the disease, disorder or condition; or
   - the feasibility of making a collaboration or consortium or other arrangements to include representation.
3. Some minority groups or subgroups are excluded or poorly represented because the purpose of the research constrains the applicant's selection of study subjects by race or ethnicity (e.g., uniquely valuable cohorts, stored specimens or existing datasets are of limited minority representation, 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).
4. Racial or ethnic origin of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens or data sets with incomplete racial or ethnic documentation are used) and this does not compromise the scientific objectives of the research.

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 whether clinically important sex/gender and/or race/ethnicity differences are expected from the intervention effect. The discussion may include supporting evidence and/or data derived from animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies, and observational, natural history, epidemiology and other relevant studies. The discussion of expected sex/gender and/or race/ethnicity differences in intervention effect must include selection and discussion of one of the following analysis plans:

- Plans to conduct valid analyses to detect significant differences in intervention effect among sex/gender and/or racial/ethnic subgroups when prior studies strongly support these significant differences among subgroups, *or*
- Plans to include and analyze sex/gender and/or racial/ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups.

(Representation of sex/gender and racial/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 and/or racial/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 Targeted/Planned Enrollment Tables for Reporting Race and Ethnicity Data for Subjects in Clinical Research

The NIH Policy on Reporting Race and Ethnicity Data for Subjects in Clinical Research is described and referenced in Section 5.8. If your application involves subprojects, attach the Targeted Enrollment Tables to the relevant subproject descriptions.

A. New Applications

All new clinical research studies should collect and report information on participants with respect to two categories of ethnicity and five categories of race. The Inclusion Enrollment Report (http://grants.nih.gov/grants/funding/phs398/phs398.html) for reporting summary data on participants to NIH includes two categories of ethnicity and five categories of race and is based on the Office of Management and Budget (OMB) reporting standards for data on race and ethnicity. Investigators should review the instructions and Frequently Asked Questions about using the Enrollment Table format at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html.

When reporting these data in the aggregate, investigators should report: (a) the number of research participants in each ethnic category; (b) the number of research participants who selected only one category for each of the five racial categories; (c) the total number of research participants who selected multiple racial categories reported as the "number selecting more than one race," and (d) the number of research participants in each racial category who are Hispanic or Latino. Investigators may provide the detailed distributions, including all possible combinations, of multiple responses to the racial designations as additional information. However, more detailed data should be compiled in a way that they can be reported using the required categories.

Instructions for Completing Targeted/Planned Enrollment Tables

Provide the study title.

The "Total Planned Enrollment" means the number of subjects that are expected to be enrolled in the study, consistent with the definition in ClinicalTrials.gov.

The "Total Planned Enrollment" will be reported in two ways in the table: by "Ethnic Category" and by "Racial Categories."

"Ethnic Category": Provide the numeric distribution of the Total Planned Enrollment according to ethnicity and sex/gender in the top part of the table.

"Racial Categories": Provide the numeric distribution of the Total Planned Enrollment, this time by racial categories and sex/gender, in the bottom part of the table. Note that Hispanic is an ethnic, not a racial, category.

If there is more than one study/protocol, provide a separate table for each.

List any proposed racial/ethnic subpopulations below the table.

Submitting Applications or Proposals Using Existing Data in Clinical Research with No Plans for Collecting New/Additional Data:

Investigators are instructed to provide plans for the total number of subjects proposed for the study and to provide the distribution by ethnic/racial categories and sex/gender using the Targeted/Planned Enrollment Tables. Under these circumstances, investigators are not required to re-contact subjects solely to comply with the newly revised categories.

If Data Collection is Ongoing, Such that New Human Subjects Will be Enrolled and/or Additional Data Will be Collected from Human Subjects:

Investigators should report ethnicity/race and sex/gender sample composition using the Inclusion Enrollment Report.

If Data Collection is Complete, Such that No New/Additional Subject Contact is Planned:

Investigators should use the Inclusion Enrollment Report.

Research Conducted at Foreign Sites:

If proposed studies involve a foreign site, investigators are encouraged to design culturally sensitive and appropriate data collection instruments that allow research participants to self-identify their racial and ethnic affiliation. However, these items should be designed in a way that they can be aggregated into the OMB-required categories. Also, the investigator can report on any racial/ethnic subpopulations by listing this information in an attachment to the required table. This may be particularly useful when distinctive subpopulations are relevant to the scientific hypotheses being studied.

When completing the Targeted/Planned Enrollment Tables that describe research in foreign sites, investigators should asterisk and footnote the table indicating that data include research participants in foreign sites. If the aggregated data only includes participants in foreign research sites, the investigator should provide information in one table with an asterisk and footnote. However, if the study includes both domestic and foreign sites, the investigator should complete two separate tables – one for domestic and another for foreign participants.

B. Renewal Application and Progress Reports

The Inclusion Enrollment Report (http://grants.nih.gov/grants/funding/phs398/phs398.html) must be used for reporting accrual data to the NIH. For Revision applications, any proposed additions to the Targeted/Planned Enrollment Tables should be provided, in addition to the Inclusion Enrollment Report. In annual progress reports, investigators conducting clinical research are required to provide the cumulative total enrollment of subjects to-date, showing the distribution by ethnic/racial categories and sex/gender on the Inclusion Enrollment Report, and must update the Targeted/Planned Enrollment Tables as needed.

4.4 Inclusion of Children

The NIH Policy on Inclusion of Children is referenced and described in Section 5.7. Instructions for item 9 of the Research Plan are as follows:

- Create a section entitled “Inclusion of Children” and place it immediately following the Targeted/Planned Enrollment Table.
- For the purpose of implementing these guidelines, a *child* is defined as an individual under the age of 21 years (for additional information see http://grants.nih.gov/grants/funding/children/children.htm and http://grants.nih.gov/grants/guide/notice-files/not98-024.html).
- Provide either a description of the plans to include children, or, if children will be excluded from the proposed research, application, or proposal, present an acceptable justification for the exclusion (see below).

- If children are included, 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.
- 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.
- 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, all individuals under 21 are considered children; however, exclusion of any specific age group, such as individuals under 18, should be justified in this section. It is expected that children will be included in all clinical research unless one or more of the following exclusionary circumstances apply:

1. The research topic to be studied is not relevant to children.
2. Laws or regulations bar the inclusion of children in the research.
3. 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.
4. A separate, age-specific study in children is warranted and preferable. Examples include:
   a. 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
   b. The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
   c. 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.
5. 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.
6. 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).
7. Other special cases can be justified by the investigator and found acceptable to the review group and the Institute/Center Director.

5. Human Subjects Research Policy

Human Subjects Research Policy includes DHHS 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 (DHHS) 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 DHHS. The regulations stipulate that the awardee organization, whether domestic or foreign, bears responsibility for safeguarding the rights and welfare of human subjects in DHHS-supported research activities. The regulations require that all organizations engaged in nonexempt human subjects research supported or conducted by the DHHS hold a Federal-wide 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; email: ohrp@osophs.dhhs.gov. In general, OHRP considers organizations that receive direct support from DHHS 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/index.html#engagement). 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 a DHHS 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 under the specific FWA has reviewed and approved the proposed activity in accordance with the DHHS 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 DHHS 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 DHHS 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 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 DHHS 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." The NIH Office of Extramural Research Human Subjects website contains additional information and Frequently Asked Questions to help investigators understand how these federal requirements apply to their research. See: http://grants.nih.gov/grants/policy/hs/index.htm.

The DHHS regulations require the NIH to evaluate all applications and proposals involving human subjects (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#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.

5.2 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 website (http://www.hhs.gov/ohrp/policy/index.html).

Exemptions 1-6 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, 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. See also Part III, 2.1 Human Subjects Research.

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 under the institutional assurance with OHRP. See http://www.hhs.gov/ohrp/ to register an IRB. Certification of IRB approval must be sent to the Grants Management Office identified in the notice requesting documentation. Certification of IRB

review and approval must include: the PHS application number, title of the project, name of the program director /principal investigator, date of IRB approval, and appropriate signatures. Grantees may also use the optional form "Protection of Human Subjects - Assurance Identification/IRB Certification/Declaration of Exemption (Common Rule)" (OMB Form No. 0990-0263 http://www.hhs.gov/ohrp/humansubjects/assurance/OF310.rtf) to meet this requirement.

According to OHRP policy, in general an institution is considered to be engaged in human subjects research when it receives an NIH award to support nonexempt human subjects research. See http://www.hhs.gov/ohrp/humansubjects/assurance/engage08.htm. All institutions engaged in human subjects research must obtain a Federal Wide Assurance (FWA) from OHRP. Instructions for applying for a Federal Wide Assurance (FWA) are available from the OHRP website at http://www.hhs.gov/ohrp/assurances/assurances_index.html.

DHHS 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.hhh.gov/ohrp/humansubjects/guidance/aplrev.htm). Only the date of approval of the application should 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, the primary grantee is expected to collect the certification from each subrecipient.

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.

If more than a year will have elapsed between the initial IRB review date and the anticipated award date, the awarding unit staff shall require re-review by the IRB prior to award.

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://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp for computer-based training developed for NIH that can be downloaded at no charge. For information on facilitating education and developing curricula, see http://www.nih.gov/sigs/bioethics.

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

NIH policy requires that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving 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. All NIH-supported biomedical and behavioral research involving human subjects is defined as 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 and racial/ethnic group, and provide a rationale for selection of such subjects. 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.

5.7 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, proposals for clinical research must include a description of plans for including children. If children will be excluded from the research, the application or proposal must present an acceptable justification for the exclusion.

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.

5.8 NIH Policy on Reporting Race and Ethnicity Data: 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/ombdir15.html. 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). Reports of data on race and ethnicity shall use these categories. 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. 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, NIH uses the following definition for ethnic/racial subpopulations:

Subpopulations: 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 social-cultural implications related to the scientific question under study.

Guidance on Collecting Race and Ethnicity Data from Human Subjects

When an investigator is planning to collect data on ethnicity and race, the categories identified above should be used. The collection of greater detail is encouraged, for example on ethnic/racial subpopulations. However, any collection that uses more detail must be designed in a way that data can be aggregated into these minimally required categories. Use self-report or self-identification to collect this information by asking two separate questions – one on ethnicity and one on race. Collect ethnicity information first followed by the question on race and provide subjects with the option to select more than one racial category.

See NIH Policy on Inclusion of Women and Minorities and http://grants.nih.gov/grants/funding/women_min/women_min.htm.

5.9 Research on Transplantation of Human Fetal Tissue

In signing the application Face Page, the Authorized Organizational 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, DHHS, 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 DHHS 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, the Authorized Organizational 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.htm). See http://stemcells.nih.gov/index.asp for additional information on stem cells, and http://stemcells.nih.gov/policy/guidelines.asp for Federal policy statements and guidelines on federally funded stem cell research.

5.11 ClinicalTrials.gov Requirements

In signing the application Face Page, the Authorized Organizational 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 (see Part III, Section 2.1.6).

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 currently 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 will now 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, however, they 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 Unpaid RFA Applications and Resubmission of Applications with a Changed Grant Activity Code

See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-019.html.

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). Resubmissions of 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 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.

POLICY: This general policy on application resubmission, stated below, applies to all grant applications that might be solicited via an RFA and to instances where there is a change in activity code. There may, however, be exceptions to this policy, which will be clearly identified in the original RFA or in a follow-up RFA.

1. When an application that was submitted in response to an RFA is not funded and the investigator wishes to resubmit an application on this topic as an investigator-initiated application, it is to be submitted as a **new** application, unless provision for a resubmission application is clearly delineated in the RFA. In addition, if a subsequent RFA specifically solicits resubmissions of unfunded applications from a previous RFA, the instructions in the second RFA should be followed. In all other cases, an application submitted in response to an RFA and then resubmitted as an investigator-initiated application must be prepared as a **new** application.
2. When a previously unfunded application that was originally submitted as an investigator-initiated application is to be submitted in response to an RFA, it is to be prepared as a **new** application.
3. When an unfunded application that was reviewed for a particular research grant activity code (for example, R01) is to be submitted for a different activity code (for example, R03), it is to be prepared as a **new** application.

1.3 NIH Policy on Resubmission Applications

See: 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 submitted for the January 25, 2009 due date and beyond, NIH will accept only a single amendment (A1) to the application (called a "resubmission" application).There is no time limit for the resubmission application. Any second resubmission will be administratively withdrawn and not accepted for review. For original new and competing renewal applications submitted prior to January 25, 2009, applicants are permitted two resubmissions (A1 and A2). For these "grandfathered" applications, any second resubmission (A2) must be submitted no later than January 7, 2011, and NIH will not accept any A2 resubmissions after that date. This resubmission policy applies to all NIH extramural applications.

See NOT-OD-07-083 for special conditions and due dates for new investigator resubmission applications submitted for consecutive review cycles. Note this applies only to new investigator R01s submitted for standard receipt dates and reviewed in recurring study sections in CSR, and selected other study sections only (e.g., NOT-MH-08-002).

Although there is no time limit for the A1 resubmission, 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. PD/PIs and their institutions need to exercise their best judgment in determining the advisability of a Resubmission application after several years have elapsed.

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. Note that for the purposes of determining whether this policy applies, this $500,000 limit excludes any consortium F&A costs.

See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.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.

Applicants must seek agreement from IC staff at least six weeks prior to the anticipated submission of any application requesting $500,000 or more in direct costs for any year. Note for the purposes of determining whether or not this policy applies, this limit excludes any consortium F&A costs (see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-040.html). If the proposed budget excluding consortium F&A costs equals or exceeds the $500,000 level, then prior approval is required. 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.

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 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 Website 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 Policy for Genome-Wide Association Studies (GWAS)

NIH is interested in advancing genome-wide association studies (GWAS) to identify common genetic factors that influence health and disease through a centralized GWAS data repository. For the purposes of this policy, a genome-wide association study is defined as any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight), or the presence or absence of a disease or condition.

All applications, regardless of the amount requested, proposing a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. Data repository management (submission and access) is governed by the Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, NIH Guide NOT-OD-07-088. For additional information see: http://grants.nih.gov/grants/gwas/.

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

Several elements of an application are not required at the time the application is submitted. Instead, this information is requested later in the review cycle (i.e., “just-in-time”) to minimize burden to institutions and to ensure that the information is current. The information eligible for just-in-time submission includes:

- Current Other Support: See 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:
    - If human subjects are involved, provide the Federal-wide Assurance number (if not previously provided) and the Certification of IRB Review and Approval of the research proposed in the application, and any IRB imposed changes. Pending or out-of-date approvals cannot be accepted. IRB approval must be dated within the last year to be valid. See Part II.5.4 IRB Approval.
    - If live vertebrate animals are involved, 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 be dated within the last three years to be valid. See 2.2 Vertebrate Animals.
- Human Subjects Education: For applications that propose 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. See Required Education in the Protection of Human Research Participants in Part II, 5.5.
- Applicants for **Research Career Development Awards** will be asked to provide detailed, categorical budget and narrative justification pages (Form Page 4 and Form Page 5) prior to award.

Applicants are advised to submit just-in-time information only when requested by the awarding component. Guidance for submitting this information will be provided at the time of the request. Alternatively, this information may be submitted using the Just-In-Time feature of the eRA Commons found in the **Status** section. For information on the Commons see: https://commons.era.nih.gov/commons/index.jsp.

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. Though they sound similar, these parts of the application 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.

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.

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. Consistent with cost principles for educational institutions described in Office of Management and Budget (OMB) Circular A-21 at section J.41.b (http://www.whitehouse.gov/omb/ circulars/a021/a021.html), 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

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. See instructions in Part I, Section 4.1, item 11.

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://era.nih.gov/ElectronicReceipt/strategy_timeline.htm.

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

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.

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 (e.g., CDA and individual fellowship awards, R36, S10, and DP1). Applications submitted on the paper PHS 398 Grant Application may only include multiple PD/PIs if the option is clearly specified in the FOA.

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 Website at http://grants.nih.gov/grants/new_investigators/resources.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/resources.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 and NOT-OD-09-013 for additional information.

2. Assurances and Certifications

Each application to the PHS requires that the following assurances and certifications be verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application.

The assurances listed and explained 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.

Human Subjects Research

Research on Transplantation of Human Fetal Tissue

Research Using Human Embryonic Stem Cells

Women and Minority Inclusion Policy

Inclusion of Children Policy

ClinicalTrials.gov Requirements

Vertebrate Animals

Debarment and Suspension

Drug-Free Workplace

Lobbying

Non-Delinquency on Federal Debt

Research Misconduct

Civil Rights

Handicapped Individuals

Sex Discrimination

Age Discrimination

Recombinant DNA, including Human Gene Transfer Research

Financial Conflict of Interest

Smoke-Free Workplace

Prohibited Research

Select Agent Research

Program Director/Principal Investigator(s) Assurance

Impact of Grant Activities on the Environment and Historic Properties

Institutions Receiving Awards for Training of Graduate Students for Doctoral Degrees

2.1 Human Subjects Research

(See also Part II: Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan.)

The DHHS regulations for the protection of human 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 DHHS. The regulations stipulate that the awardee organization, whether domestic or foreign, bears responsibility for safeguarding the rights and welfare of human subjects in DHHS-supported research activities. The regulations require that all organizations engaged in nonexempt human subjects research supported or conducted by the DHHS hold a Federal-wide 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; email: ohrp@osophs.dhhs.gov. In general OHRP considers organizations that receive direct support from DHHS 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/humansubjects/guidance/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 a DHHS 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 under the specific FWA has reviewed and approved the proposed activity in accordance with the DHHS 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 DHHS 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 DHHS regulations to protect human subjects, certain research areas are exempt. (See Exemption Categories). 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 DHHS and FDA human subject protection regulations.

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/humansubjects/guidance/cdebiol.htm. For additional help determining whether research that involves the use of human data or biological specimens is human subjects research, please refer to this website: http://grants.nih.gov/grants/policy/hs/.

Vulnerable Populations

Investigators who conduct research involving pregnant women, human fetuses and neonates, prisoners (including 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 website (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.

Data and Safety Monitoring

For each proposed clinical trial, 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 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. 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 and to individual IRBs 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).

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://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp for computer-based training developed for NIH that can be downloaded at no charge. For information on facilitating education and developing curricula, see http://www.nih.gov/sigs/bioethics.

2.1.1 Research on Transplantation of Human Fetal Tissue

In signing the application Face Page, the Authorized Organizational 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, DHHS, 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 DHHS access to those records, if maintained by an entity other than the applicant organization.

2.1.2 Research Using Human Embryonic Stem Cells

In signing the application Face Page, the Authorized Organizational 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.htm). 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 also http://stemcells.nih.gov/index.asp for additional guidance on stem cells and http://stemcells.nih.gov/policy/guidelines.asp for Federal policy statements and guidelines on federally funded stem cell research.

2.1.3 NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research

NIH policy requires that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving clinical research unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant IC Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made 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. All NIH-supported biomedical and behavioral research involving human subjects is defined as 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 and racial/ethnic group, and provide the rationale for selection of such subjects. 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.

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

See NIH Policy on Reporting Ethnicity/Race and Sex/Gender in Clinical Research in Part II, 5.8.

The Office of Management and Budget (OMB) defines minimum standards for maintaining, collecting, and presenting data on race and ethnicity for all grant, contract, and intramural proposals and for all active research grants, cooperative agreements, contracts, and intramural projects. The minimum standards are described in the 1997 OMB Directive 15, http://www.whitehouse.gov/omb/fedreg/ombdir15.html.

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. See Part II, 5.8 for additional information.

2.1.5 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, proposals for clinical research must include a description of plans for including children. If children will be excluded from the research, the application or proposal must present an acceptable justification for the exclusion.

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.

2.1.6 ClinicalTrials.gov

In signing the application Face Page, the Authorized Organizational Representative of the applicant organization assures compliance with Public Law 110-85, enacted 09/27/2007, if applicable (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf). The law amends the Public Health Service Act to expand the scope of clinical trials that must be registered in ClinicalTrials.gov. It also increases the number of registration fields that must be submitted, requires certain results information to be included, and sets penalties for noncompliance.

The trials that must be registered are called "applicable clinical trials." 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. NIH encourages registration of ALL trials whether required under the law or not.

The entity responsible for registering the trial is the "responsible party."

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

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

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 the Office of Laboratory Animal Welfare (OLAW) at the time of award for all grantee organizations receiving PHS support to conduct research

using 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. These documents are available from the Office of Laboratory Animal Welfare, National Institutes of Health, Bethesda, MD 20892, (301) 496-7163 (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 including custom antibody preparation.

In addition to an approved Animal Welfare Assurance, the grantee organization must provide verification that the Institutional Animal Care and Use Committee (IACUC) has reviewed and approved the proposed activity. IACUC approval must be dated within the last three years in order 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 Assurance.

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.

If the prime grantee does not have an Animal Welfare Assurance and the animal work will be conducted at an institution with an Assurance, the grantee must obtain an Inter-institutional Assurance from OLAW. 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 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 Council for International Organizations of Medical Sciences' *International Guiding Principles for Biomedical Research Involving Laboratory Animals* (http://www.cioms.ch/frame_1985_texts_of_guidelines.htm) and all laws, regulations and policies governing the care and use of laboratory animals in the jurisdiction in which the research will be conducted.

2.3 Debarment and Suspension

Executive Order 12549, "Debarment and Suspension," mandated development of a Government-wide debarment and suspension system for nonprocurement transactions with Federal agencies. Executive Order 12689 and Section 2455 of the Federal Acquisition Streamlining Act of 1994 further required Federal agencies to establish regulations for reciprocal Government-wide effect across procurement

and nonprocurement debarment and suspension actions. This reciprocity rule is effective for any debarment, suspension or other Government-wide exclusion initiated on or after August 25, 1995.

DHHS regulations implementing Executive Orders 12549 and 12689 and Section 2455 of the Federal Acquisition Regulation are provided in 2 CFR 180 and 376, “Government-wide Debarment and Suspension (Nonprocurement).” Changes in this Government-wide requirement implement this as a term and condition of an award.

2.4 Drug-Free Workplace

DHHS regulations implementing the Drug-Free Workplace Act of 1988 (Public Law 100-690, Title V, Subtitle D) are now provided in 45 CFR 82, “Government-wide Requirements for Drug-Free Workplace (Financial Assistance).” Changes in this Government-wide requirement (adopted in the November 26, 2003 Federal Register Notice) now implement this as a term and condition of an award.

2.5 Lobbying

a) Title 31, United States Code, Section 1352, entitled “Limitation on Use of Appropriated Funds to Influence Certain Federal Contracting and Financial Transactions,” generally prohibits recipients of Federal grants and cooperative agreements from using Federal (appropriated) funds for lobbying the Executive or Legislative Branches of the Federal Government in connection with a specific grant or cooperative agreement. Section 1352 also requires that each person who requests or receives a Federal grant or cooperative agreement must disclose lobbying undertaken with non-Federal (nonappropriated) funds. These requirements apply to grants and cooperative agreements exceeding $100,000 in total costs. DHHS regulations implementing Section 1352 are provided in 45 CFR Part 93, “New Restrictions on Lobbying.”

The complete Certification Regarding Lobbying is provided below:

> “The undersigned (authorized official signing for the applicant organization) certifies, to the best of his or her knowledge and belief that:
>
> (1) No Federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with the awarding of any Federal contract, the making of any Federal grant, the making of any Federal loan, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal contract, grant, loan, or cooperative agreement.
>
> (2) If any funds other than Federally appropriated funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal contract, grant, loan, or cooperative agreement, the undersigned shall complete and submit Standard Form LLL, “Disclosure of Lobbying Activities,” in accordance with its instructions.
>
> (3) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers (including subcontracts, subgrants, and contracts under grants, loans and cooperative agreements) and that all subrecipients shall certify and disclose accordingly.
>
> This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by section 1352, U.S. Code. Any person who fails to file

the required certification shall be subject to a civil penalty of not less than $10,000 and not more than $100,000 for each such failure."

Standard Form LLL, "Disclosure of Lobbying Activities," its instructions, and continuation sheet are available from GrantsInfo, National Institutes of Health, e-mail: GrantsInfo@nih.gov, (301) 435-0714.

b) Organizations described in section 501(c)4 of the Internal Revenue Code of 1968 that engage in lobbying are not eligible to receive grant/cooperative agreement awards. This is not to be confused with 45 CFR Part 93, Section 1352, New Restrictions on Lobbying.

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 organizational official 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 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 DHHS Office for Civil Rights: an Assurance of Compliance (Form DHHS 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 DHHS 690 is available from http://www.hhs.gov/forms/HHS690.pdf.

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

2.9 Research Involving Recombinant DNA, including Human Gene Transfer Research

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. As defined by the *NIH Guidelines,* recombinant DNA molecules are either: (1) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell; or (2) DNA molecules that result from the replication of those described in (1).

The *NIH Guidelines* set forth principles and standards for safe and ethical conduct of recombinant DNA research and apply to both basic and clinical research studies. The *NIH Guidelines* should be carefully reviewed and implemented to ensure that proper biosafety and containment practices are employed for all projects involving recombinant DNA research, including review by an Institutional Biosafety Committee that meets the requirements of the *NIH Guidelines*. More information about the NIH Guidelines and IBCs can be found at: http://oba.od.nih.gov/rdna_ibc/ibc.html. Further, the *NIH Guidelines,* in Appendix M, include special review and reporting requirements for the conduct of human gene transfer studies. Failure to comply with the *NIH Guidelines* may result in suspension, limitation, or termination of NIH funds for recombinant DNA research at the organization or a requirement for NIH prior approval of any or all recombinant DNA projects at the organization. A copy of the NIH Guidelines is posted at the following URL: http://oba.od.nih.gov/rdna/nih_guidelines_oba.html and may be obtained from the NIH Office of Biotechnology Activities, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892, 301-496-9838. Additional information on the special requirements that pertain to human gene transfer can be found in a series of Frequently Asked Questions at: http://oba.od.nih.gov/rdna/rdna_faq_list.html.

2.10 Financial Conflict of Interest

NIH requires grantees and investigators (except Phase I SBIR/STTR applicants) 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.” These requirements promote objectivity in research by establishing standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research funded under PHS grants or cooperative agreements will be biased by any conflicting financial interest of an investigator.

The signature of the authorized organizational official on the Face Page of the application serves as certification of compliance with the requirements of 42 CFR Part 50, Subpart F, including that:

1. There is in effect at the organization a written and enforced administrative process to identify and manage, reduce, or eliminate conflicting financial interests with respect to research projects for which NIH funding is sought.
2. Prior to the expenditure of any NIH funds awarded under a new award, the organization will inform NIH of the existence of any conflicting financial interests of the type covered by 42 CFR 50.605 and assure that the interest has been managed, reduced, or eliminated in accordance with the regulations.
3. The Institution will continue to make similar reports on subsequently identified conflicts within 60 days of identification.
4. When the Institution determines that a financial conflict of interest exists (see #2 and #3 above), the institution must notify the NIH through the FCOI module in the eRA Commons of its existence and provide the following information:
   - Grant number and Principal Investigator;
   - Name of Investigator with FCOI; and
   - Distinguish which method was used to protect the involved PHS funded research from bias (i.e., managed, reduced, or eliminated).
5. When requested, the institution will make information available to NIH regarding all identified conflicting interests and how those interests have been managed, reduced, or eliminated to protect the research from bias.

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 110-005 that authorizes NIH appropriations:

BAN ON FUNDING OF HUMAN EMBRYO RESEARCH

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/index.asp.

LIMITATION ON USE OF FUNDS FOR PROMOTION OF LEGALIZATION OF CONTROLLED SUBSTANCES

"(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

"Notwithstanding any other provision of this Act, no funds appropriated under 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

"(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."

2.13 Select Agent Research

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (P.L. 107-188) 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 CDC at 42 CFR 73 http://www.cdc.gov/od/sap/pdfs/42_cfr_73_final_rule.pdf, Select Agents and Toxins.

As a term of award, grantees who conduct research involving Select Agents (see 42 CFR 73 for the list; and 7 CRF 331 and 9 CFR 121 for the relevant animal and plant pathogens) are reminded that they must complete registration with CDC (or USDA, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

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

For additional information regarding Select Agent research, see the following websites maintained by NIH, CDC, and USDA:

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

Center for Disease Control Select Agent Program:
http://www.cdc.gov/od/sap/index.htm

Center for Disease Control Select Agent Program Guidelines:
http://www.cdc.gov/od/sap/guidelines.htm

Center for Disease Control Select Agent Program Public Laws and Regulations:
http://www.cdc.gov/od/sap/regulations.htm

Center for Disease Control Select Agent Program Related Links:
http://www.cdc.gov/od/sap/regulations.htm

Animal and Plant Health Inspection Service (APHIS) Select Agent Program:
http://www.aphis.usda.gov/programs/ag_selectagent/

2.14 Program Director/Principal Investigator 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 DHHS 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.

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 (ACT), 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. 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 Construction Grants – Public Policy Requirements and Objectives.

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).

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.

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.

Animal. Any live vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes at the applicant organization, any collaborating site, or other Project/Performance Site.

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: 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 independently owned and operated, is not dominant in the field of operation in which it is proposing, has its principal place of business located in the United States, and is organized for profit.
2. Is at least 51% owned and controlled by either: (a) one or more natural persons (individuals who are citizens of, or permanent resident aliens in, the United States); or (b) another for-profit business concern that is itself at least 51% owned and controlled by one or more natural persons (individuals who are citizens of, or permanent resident aliens in, the United States)(See 13 CFR 121.105 (defining “business concern”)).
3. Has, including its affiliates, *a number of employees not exceeding 500*, and meets the other regulatory requirements found in 13 CFR Part 121. Business concerns, other than investment

companies licensed, or state development companies qualifying under the Small Business Investment Act of 1958, 15 U.S.C. 661, et seq., are affiliates of one another when either directly or indirectly, (a) one concern controls or has the power to control the other; or (b) a third-party/parties controls or has the power to control both.

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: 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: A small business concern that is at least 51% owned by a woman or women who also control and operate it. "Control" in this context means exercising the power to make policy decisions. "Operate" in this context means being actively involved in the day-to-day management.

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 *Grants Policy Statement*.

Commercialization. The process of developing markets and producing and delivering products for profit (whether by the originating party or by others). As used here, commercialization includes both government and private sector markets.

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*.

Cooperative Agreement. A financial assistance instrument under which substantial Federal involvement is anticipated between the Federal agency and the recipient during performance of the contemplated project or activity. "Substantial involvement" means that the recipient can expect Federal programmatic collaboration or participation in carrying out the effort under the award.

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.

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.

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

Foreign Component. A component of a grant to a domestic organization that provides support to any significant element or segment of the project to be performed outside the United States (including the involvement of human subjects or laboratory animals; extensive foreign travel for the purpose of data collection, surveying, sampling, and similar activities: and any activity of the recipient that may involve the population, environment, resources, or affairs of a foreign country), either by the recipient's project staff or individuals employed by a foreign organization (for example, under a contract or a consortium agreement). Foreign travel for consultation is not considered a foreign component.

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.

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.

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 defines a child as an individual under the age of 21 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.

DHHS 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 prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective.

Behavioral human subjects research involving an intervention to modify behavior (diet, physical activity, cognitive therapy, etc.) fits this definition of a clinical trial.

Human subjects research to develop or evaluate clinical laboratory tests (e.g. imaging or molecular diagnostic tests) might be considered to be a clinical trial if the test will be used for medical decision making for the subject or the test itself imposes more than minimal risk for subjects.

Biomedical clinical trials of experimental drug, treatment, device or behavioral intervention may proceed through four phases:

> ***Phase I*** clinical trials test a new biomedical intervention in a small group of people (e.g., 20-80) for the first time to evaluate safety (e.g., to determine a safe dosage range and to identify side effects).
>
> ***Phase II*** clinical trials study the biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and to further evaluate its safety.
>
> ***Phase III*** studies investigate the efficacy of the biomedical or behavioral intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.
>
> ***Phase IV*** studies are conducted after the intervention has been marketed. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

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 DHHS 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/humansubjects/guidance/cdebiol.pdf.)

Data and Safety Monitoring Plan. For each clinical trial, 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 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*.

Exemptions. The six categories of research exempt from the DHHS 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/humansubjects/guidance/decisioncharts.htm) 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 website 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 targeted/planned enrollment tables, 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.

Gender. Refers to the classification of research subjects into either or both of two categories: male and female. In some cases, representation is unknown because gender composition cannot be accurately determined (e.g., pooled blood samples or stored specimens without gender designation).

Human Subjects. The DHHS 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/humansubjects/guidance/cdebiol.pdf.)

Research. DHHS 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.

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/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 among the gender and racial/ethnic groups.

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.

Mechanism. 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.

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/resources.htm.

See also the definition of Early Stage Investigator.

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.

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.

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 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 principal investigators (PD/PIs) who share the authority and responsibility for leading and directing the project, intellectually and logistically. When multiple principal investigators are named, each 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 PD/PI on an application or award diminishes neither the responsibility nor the accountability of any individual PD/PI.

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.

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

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.

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).

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.

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 website 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://era.nih.gov/ElectronicReceipt/strategy_timeline.htm .

For more information on NIH's transition plans, see the website for Electronic Submission of Grant Applications: http://era.nih.gov/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).
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.
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) http://grants.nih.gov/training/nrsa.htm	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 Privacy Act of 1974 (5 U.S.C. 552a) is a records management statute and regulates the collection, maintenance, use, and dissemination of personal information by Federal agencies. In accordance with the Act, the PHS is required to provide the following notification to each individual whom it asks to supply information.

The PHS maintains applications and grant records pursuant to its statutory authority for awarding grants. The purpose of the information collection is to aid in the review, award, and administration of PHS programs. Provision of information is voluntary; however, a lack of sufficient information may hinder the ability of the PHS to review applications, monitor grantee performance, or perform overall management of grant programs. Please be aware that no individual will be denied any right, benefit, or privilege provided by law because of refusal to disclose this section of the Social Security Number. The PHS requests the last four digits of the Social Security Number under Sections 301(a) and 487 of the PHS Acts as amended (42 U.S.C 241a and U.S.C. 288). All analyses conducted on the date of birth, gender, race and/or ethnic origin data will report aggregate statistical findings only and will not identify individuals. If you decline to provide this information, it will in no way affect consideration of your application.

The Privacy Act authorizes discretionary disclosure of this information within the Department of Health and Human Services and outside the agency to the public, as required by the Freedom of Information Act and the associated DHHS regulations (45 CFR 5), including the Congress acting within its legislative authority, the National Archives, the General Accounting Office, the Bureau of Census, law enforcement agencies, and pursuant to a court order. Information also may be disclosed outside the Department, if necessary, for the following purposes:

1. To a Congressional office at the request of the record subject;
2. To the Department of Justice as required for litigation;
3. To the cognizant audit agency for auditing;
4. To qualified experts not within the definition of Department employees as prescribed in Department Regulations (45 CFR 5b.2) for opinions as part of the application review/award process;
5. For an authorized research purpose under specified conditions;
6. To contractors for the purpose of processing, maintaining, and refining records in the system. Contractors will be required to maintain Privacy Act safeguards with respect to such records;
7. To a Federal agency, in response to its request, in connection with the letting of a contract, or the issuance of a license, grant, or other benefit by the requesting agency, to the extent that the records are relevant and necessary to the requesting agency's decision on the matter; and
8. To the applicant organization in connection with the review of an application or performance or administration under the terms and conditions of the award, or in connection with problems that might arise in performance or administration if an award is made.

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.

The Freedom of Information Act and implementing DHHS regulations (45 CFR Part 5) require the release of certain grant documents and records when requested by the public, regardless of the intended use of the information. These policies and regulations apply to information in the possession of NIH and generally do not require grantees to permit access to their records except as described in 4.6 Access to Research Data, below. Generally available for release upon request are: all funded grant applications and progress reports including their derivative funded noncompeting supplemental grant progress reports; pending and funded noncompeting 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 DHHS. Generally **not** available for release to the public are: competing grant progress reports (new, Renewal, and Revision) 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. 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 74.36, 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 a Federal 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 educational institution, 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.