U.S. Department of Health and Human Services

Public Health Service

Grant Application (PHS 398)

PART II

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

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PREPARING THE HUMAN SUBJECTS RESEARCH SECTION OF THE RESEARCH PLAN

To assist you in completing Item e. of the Research Plan (Human Subjects Research), we have provided six possible scenarios. All research will fall into one of these six scenarios. Determining which scenario best matches your proposed research depends on your answers to the following five questions:

Question 1: Does your proposed research involve human subjects?

Question 2: Is your proposed research described by one or more of the exemptions in the HHS regulations (45 CFR Part 46)?

Question 3: Does your proposed research meet the definition for clinical research?

Question 4: Does your proposed research include a Clinical Trial?

Question 5: Does your proposed research meet criteria for an NIH-Defined Phase III Clinical Trial?

Click on the questions and when you can answer the five questions, select the scenario that best matches your responses, and then follow the instructions provided for the scenario you choose.

In the Human Subjects Research section of the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets (1) the requirements of the HHS regulations to protect human subjects from research risks (45 CFR Part 46), and (2) the requirements of NIH policies on inclusion of women, minorities, and children. See Instructions Pertaining to Non-Exempt Human Subjects Research.

If the research is exempt from the requirements in the Federal regulations, you must provide a justification for the exemption with 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. See Exempt Research.

Applications must comply with this requirement; if not, application processing may be delayed or the application may be returned to the applicant without review.

For all research involving human subjects, a part of the peer review process will include careful consideration of protections from research risks, as well as the appropriate inclusion of women, minorities, and children. The Scientific Review Group (SRG) will assess the adequacy of safeguards of the rights and welfare of research participants, and the appropriate inclusion of women, minorities, and children, based on the information in the application.

HUMAN SUBJECTS RESEARCH

Question 1: Does your proposed research involve human subjects?

The first thing you must determine is whether or not your research involves human subjects, either at the applicant organization or at any other performance site or collaborating institution (e.g., subcontractors, consultants).

Federal regulations (45 CFR Part 46) 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

The definition of human subjects includes the use of human organs, tissues, and body fluids, as well as graphic, written, or recorded information, from living individuals if the identity of the subjects can be readily ascertained by the investigator or other members of the research team.

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.

Interaction includes communication or interpersonal contact between investigator and subject.

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 which has been provided for specific purposes by an individual and which 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.

Regulatory requirements (Federal and state) to protect human subjects apply to a much broader range of research than many investigators realize, and researchers using human tissue specimens are often unsure about how regulations apply to their research. Regulatory obligations to protect human subjects *may* apply, for example, to research that uses –

- Bodily materials, such as cells, blood or urine, tissues, organs, hair or nail clippings, from identifiable living individuals, even if you did not collect these materials
- Residual diagnostic specimens, from identifiable living individuals, including specimens obtained for routine patient care that would have been discarded if not used for research
- Private information, such as medical information, that can be readily identified with living individuals, even if the information was not specifically collected for the study in question. This includes research on cell lines or DNA samples that can be readily associated by the investigator or others engaged in the research with the identity of living individuals.

Cadaver Specimens: If your research proposes the use of cadaver specimens, then the answer to question 1 is "No" because human subjects are defined as "living individuals." The use of cadaver specimens is governed by applicable state and local law and is not directly regulated by 45 CFR Part 46.

Guidance and Additional Instructions

If you answered “No” to Question 1, then proceed to Scenario A.

If activities involving human subjects are planned at any time during the proposed project period, either at the applicant organization or at any other performance site or collaborating institution, then your answer is “Yes” even if the research is exempt from regulations for the protection of human subjects.

If you answered “Yes” to Question 1, then you may need to determine whether your research meets the criteria for an exemption from the Human Subjects Protection requirements. Proceed to Question 2.

If you need to consider an alternative scenario, return to the PHS 398 Instructions Decision Table for Section e.

EXEMPT RESEARCH

Question 2: Is your proposed research described by one or more of the exemptions in the HHS regulations (45 CFR Part 46)?

Some human subjects research is exempt from the HHS regulations (45 CFR Part 46). Read descriptions of the following six exemptions to determine if your research meets the criteria for one or more of the following exemptions. In order to be exempt, the involvement of human subjects in the research activities must be limited to only one or more of the categories of exempt research.

OHRP advises that the IRB (or some authority other than the investigator) determines whether proposed research is exempt from the HHS human subjects regulations.

Research involving individuals who are or who become prisoners cannot be exempt under any exemption categories (see 45 CFR Part 46 Subpart C).

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 involving 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.

Research that meets the criteria for Exemption 4 is not considered “clinical research.”

Evaluating what does and does not fall under Exemption 4 can be complex. The NIH brochure, Research on Human Specimens, contains information that is helpful in making this determination. See http://www.cancerdiagnosis.nci.nih.gov/specimens/brochure.html and also the information contained at: Exemption 4 Guidance and Information.

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.

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.

Guidance and Additional Instructions

If you answered "Yes" to Question 2, then your research meets the criteria for an exemption.

- If your research meets the criteria for Exemption 4, then follow the instructions for Scenario B and read the information contained in Exemption 4 Guidance and Information.
- If your research meets the criteria for any of the other five exemptions, follow the instructions for Scenario C.

Remember that you need to identify which exemption(s) you believe is applicable to your research, and provide a justification for the exemption(s) with sufficient information about the involvement of human subjects to allow a determination by peer reviewers and NIH staff that the claimed exemption(s) is appropriate.

If you answered "No" to Question 2, then your research does not qualify for one of the exemptions, and your research is not exempt from full IRB review. Proceed to Question 3.

If you need to consider an alternative scenario, return to the PHS 398 Instructions Decision Table for Section e.

CLINICAL RESEARCH

Question 3: Does your proposed research meet the definition for clinical research?

The NIH defines Clinical Research as:

(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.

Clinical research that does not meet the criteria for a clinical trial or an NIH-defined Phase III clinical trial must follow the instructions in Scenario D.

Research that meets the criteria for Exemption 4 is not considered "clinical research." Investigators with research that meets the criteria for Exemption 4 must follow the instructions provided in Scenario B.

Guidance and Additional Instructions

If you answered "Yes" to Question 3, then proceed to Question 4 and Question 5 to determine whether your research meets the criteria for a clinical trial or an NIH-defined Phase III clinical trial.

If you answered "No," then you need to consider an alternative Scenario. Return to the PHS 398 Instructions Decision Table for Section e.

CLINICAL TRIAL

Question 4: Does your proposed research include a 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 these criteria 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.

Guidance and Additional Instructions

If you answered “Yes” to Question 4, then you will need to provide a general description of a Data and Safety Monitoring Plan. See Scenario E.

Also continue to Question 5 to determine whether your research meets the criteria for an NIH-defined Phase III clinical trial.

If you answered “Yes” to Question 3 (Clinical Research) and “No” to Question 4 (Clinical Trial), then follow the instructions for Scenario D.

If you answered “No” to Question 4, you will need to consider an alternative scenario. Return to the PHS 398 Instructions Decision Table for Section e.

NIH-DEFINED PHASE III CLINICAL TRIAL

Question 5: Does your proposed research meet criteria for an 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 either evaluating an experimental intervention in comparison with a standard or control intervention or of 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.

If your research meets the above criteria, then in addition to providing a Data and Safety Monitoring Plan, you will be expected to address whether you expect to find clinically important sex/gender and/or race/ethnicity differences in the intervention effect. The discussion may include supporting evidence and/or data derived from prior animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies, and observational, natural history, epidemiology, and other relevant studies.

You will be expected to provide a research plan that must include one of the following 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 between subgroups.

Guidance and Additional Instructions

If you answered “Yes” to Question 5, then follow the instructions for Scenario F.

If you answered “No,” then you need to consider an alternative Scenario. Return to the PHS 398 Instructions Decision Table for Section e.

EXEMPTION 4 GUIDANCE AND INFORMATION

Research that meets the criteria for Exemption 4 is Human Subjects Research, but it is not considered clinical research. Evaluating what does and does not fall under Exemption 4 can be complex. The NIH Brochure, "Research on Human Specimens," (http://www.cancerdiagnosis.nci.nih.gov/specimens/brochure.html) is helpful in making this determination.

Exemption 4 includes 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.

NOTE: Some researchers mistakenly believe that any studies on existing pathology specimens are exempt. Exemption 4 does not apply to specimens that are linked to patient identity, even if the subject identifiers are locked up or kept by someone other than the researcher. It does not matter if the tissue would otherwise have been discarded. OHRP strongly recommends that investigators should not have the authority to make an independent determination that research involving human subjects is exempt. Investigators should check with the IRB or other designated authorities to determine institutional policies and procedures for the designation of any exemptions claimed for the proposed research (see http://www.hhs.gov/ohrp/humansubjects/guidance/hsdc95-02.htm).

What is meant by "existing" data or specimens?

Exemption 4 applies to retrospective studies of specimens that have already been collected. The materials must be "on the shelf" (or in the freezer) at the time the protocol is submitted to the IRB or other designated officials at your institution to determine whether the research is indeed exempt. Prospective collection of additional specimens does not meet the criteria for Exemption 4.

What about specimens obtained from a tissue bank?

OHRP offers guidance about the requirements for establishing tissue banks and repositories to collect, store, and distribute human tissue materials for research purposes (see current guidance at http://www.hhs.gov/ohrp/policy/index.html). There are many kinds of tissue banks that operate in different ways. Use of tissue specimens obtained from an established tissue repository may be exempt under certain circumstances. You should check with your IRB or other designated authorities at your institution to determine how the exemption applies to your research.

What is meant by "publicly available sources"?

This language in the regulation was intended to apply to public sources of data, such as census data. Its meaning with respect to human tissue specimens is widely debated. Although there are organizations that make human cells and tissues broadly accessible at reasonable cost to the research community, these materials are not usually available to the public at large.

What is meant by "identifiers linked to the subjects"?

Identifiers, such as names, social security numbers, medical record numbers, or pathology accession numbers, permit specimens to be linked to living individuals and perhaps also to associated medical information.

Exemption 4 may apply to specimens provided by a tissue bank or other repository, so long as the specimens are provided without identifiers and the repository has firm policies and procedures, approved by its own IRB, to prevent the release of personal information.

Exemption 4 does not apply in situations where a researcher receives “coded” specimens from a collaborator if the collaborator retains the key to the code, even though the researcher may have no access to patient identities.

How can I determine whether my research meets the criteria for Exemption 4?

The humans subjects regulations decision charts (http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm) from the Office of Human Research Protection (OHRP) will help you to see whether your research falls under the human subjects regulations and if so, whether it meets the criteria for Exemption 4. OHRP advises that investigators should not have the authority to make an independent determination that research involving human subjects is exempt. Investigators should check with the IRB or other designated authorities to determine institutional policies and procedures for the designation of any exemptions claimed for the proposed research (see http://www.hhs.gov/ohrp/humansubjects/guidance/hsdc95-02.htm).

Guidance and Additional Instructions

If your research meets the criteria for Exemption 4, refer to Scenario B.

If you need to consider an alternative scenario, return to the PHS 398 Instructions Decision Table for Section e.

INSTRUCTIONS PERTAINING TO NON-EXEMPT HUMAN SUBJECTS RESEARCH

In your application narrative, create a section entitled “e. Human Subjects Research” immediately following the last entry in the Research Design and Methods section. 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.

As the first entry, create a heading entitled “Human Subjects Research and Protection from Risk.” Use subheadings to address the issues listed under items 1-4 below.

If your research includes a clinical trial, create another section heading entitled "Data and Safety Monitoring Plan." Instructions follow items 1-4.

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1. RISKS TO THE SUBJECTS

a. Human Subjects Involvement and Characteristics

- Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section.
- Describe the characteristics of the subject population, including their anticipated number, age range, and health status.
- Identify the criteria for inclusion or exclusion of any subpopulation.
- Explain the rationale for the involvement of special classes of subjects, 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.
- List any collaborating sites where human subjects research will be performed, and describe the role of those sites in performing the proposed research.

b. Sources of Materials

- Describe the research material obtained from living human subjects in the form of specimens, records, or data.
- Describe any data that will be recorded on the human subjects involved in the project.
- Describe the linkages to subjects, and indicate who will have access to subject identities.
- Provide information about how the specimens, records, or data are collected and whether material or data will be collected specifically for your proposed research project.

c. Potential Risks

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

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. Informed consent document(s) need not be submitted to the PHS agencies unless requested.

b. Protection Against Risk

- Describe planned procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness.
- 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 description of the plan for data and safety monitoring of the research and adverse event reporting to ensure the safety of subjects.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

- Discuss the potential benefits of the research to the subjects and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.

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 biologicals) 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 Food and Drug Administration, and/or the status of requests for an IND or IDE covering the proposed use of the test article in the research plan.

DATA AND SAFETY MONITORING PLAN

- If your research includes a clinical trial, create a section 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:
  - Principal Investigator (required)
  - Independent individual/Safety Officer
  - Designated medical monitor
  - Internal Committee or Board with explicit guidelines
  - Data and Safety Monitoring Board (DSMB – specifically required for multi-site trials involving interventions that entail potential risk to the participants)
  - Institutional Review Board (IRB - required)
- 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 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html). For additional guidance on creating this Plan, see the above reference.

DATA AND SAFETY MONITORING BOARD

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 use DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.

Guidance and Additional Instructions

Proceed to Inclusion of Women and Minorities.

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH

Create a section heading entitled "Inclusion of Women and Minorities" and place it immediately following the “Human Subjects Research” section. 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.

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.) If you are using existing specimens and/or data that does not meet the criteria for Exemption 4 and you do not have 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 is inappropriate (item 3 below). Alternatively, you may describe the women and minority composition of the population base from whom the specimens and/or data will be obtained. Include the Targeted/Planned Enrollment Table (MS Word or PDF) 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.

Examples of acceptable justifications for 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;
        - 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;
   - 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;
   - 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.

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

If your proposed research includes an NIH-Defined Phase III Clinical Trial, the section on Inclusion of Women and Minorities also must address whether you expect to find clinically important sex/gender and/or race/ethnicity differences in the intervention effect. The discussion may include supporting evidence and/or data derived from prior animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies, and observational, natural history, epidemiology and other relevant studies. Your 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 between subgroups.

Instructions for Completing the Targeted/Planned Enrollment Tables for Reporting Race and Ethnicity Data for Subjects in Clinical Research

A. New Applications and Clinical Research Studies begun after January 10, 2002:

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 new Inclusion Enrollment Report Table (MS Word or PDF) for reporting summary data on participants to NIH includes two categories of ethnicity and five categories of race and is based on recent changes by the Office of Management and Budget (OMB) regarding standards for data on race and ethnicity. Investigators should review the instructions and Frequently Asked Questions about using the new 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 respondents in each ethnic category; (b) the number of respondents who selected only one category for each of the five racial categories; (c) the total number of respondents who selected multiple racial categories reported as the "number selecting more than one race," and (d) the number of respondents 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 items should be designed in a way that they can be aggregated into the required categories for reporting purposes.

For new applications and clinical research studies begun after January 10, 2002, use the Targeted/Planned Enrollment Table format (MS Word or PDF).

Provide the study title.

The '"Total Planned Enrollment" means the number of subjects that are expected to be enrolled during the entire period of the study and are needed to evaluate the research question 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 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.

How should I report race and ethnicity data when my research involves a foreign population?

Investigators are encouraged to design their data collection instruments in ways that allow respondent self-identification of their racial and ethnic affiliation. However, these items should be designed in a way that they can be aggregated into the 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 tables, investigators should asterisk and footnote the table indicating that data includes foreign participants. If the aggregated data only includes foreign participants, the investigator should provide information in one table with an asterisk and footnote. However, if the study includes both domestic and foreign participants, we suggest the investigator complete two separate tables – one for domestic data and one for foreign data, with an asterisk and footnote accompanying the table with foreign data.

B. Clinical Research Studies begun before January 10, 2002:

If the proposed research uses existing data, then use the formats below for competing continuations and competing supplements. Investigators should review the instructions and Frequently Asked Questions about using the new Enrollment Table format at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html.

Competing Continuations:

For competing continuations involving the collection of new/additional clinical data, use the "Targeted/Planned Enrollment Table (MS Word or PDF)" and the instructions above. **Note:** If you choose to report information with the new Targeted/Planned Enrollment Table, you must continue to use this format for the remaining years of the project.

For competing continuations involving studies begun before January 10, 2002 that do not involve the collection of new/additional clinical data, the data on ethnicity/race and sex/gender may be presented in EITHER the Targeted/Planned Enrollment Table (MS Word or PDF) OR the 4/98 Version of the Inclusion Table (MS Word or PDF). If data were originally collected from study subjects using two questions (one about ethnicity and one about race) and subjects were given the option of selecting more than one race, then use the Targeted/Planned Enrollment Table. Otherwise, use the 4/98 Version of the Inclusion Table, which uses a combined race/ethnicity format with five categories.

Competing Supplements:

For competing supplemental applications involving studies begun before January 10, 2002, investigators may report ethnicity/race and sex/gender composition using EITHER the Inclusion Enrollment Report (MS Word or PDF) OR the 4/98 Version of the Inclusion Table (MS Word or PDF). If data are being collected using two questions (one about ethnicity and one about race) and subjects were given the option of selecting more than one race, then use the Targeted/Planned Enrollment Table. **Note:** If you choose to report information with the new Targeted/Planned Enrollment Table, you must continue to use this format for the remaining years of the project.

If data are being collected using one question that combines ethnicity and race, use the 4/98 Version of the Inclusion Table. For previously funded studies that used the 4/98 Version of the Inclusion Table the earlier reporting format is NOT directly transferable to the format.

C. What Inclusion/Enrollment Table Should Principal Investigators Use for Reporting Accrual Data to NIH? (New versus Old Table)

The following instructions apply to progress reports, whether submitted as part of a non-competing or competing application.

Guidelines for choosing the new Inclusion Enrollment Report Table versus the old Inclusion Table are as follows:

New Inclusion Enrollment Report (MS Word or PDF)

- Studies begun after January 10, 2002, must be designed to ask participants two questions, one about their ethnicity and one about their race, and investigators must use the new Inclusion Enrollment Report table format for reporting summary data to NIH.

- Principal investigators who started a study prior to January 10, 2002 using the old Inclusion Table format for reporting summary data to NIH may switch to the new Inclusion Enrollment Report format if they choose to do so, but they must also change their data collection methods to ask two questions (one about ethnicity and another about race) rather than one question (that combined race and ethnicity) for all participants enrolled in the study from that point on.

- For studies that began prior to January 10, 2002: When the study is submitted for competing continuation (Type 2) and plans to collect new/additional data, the principal investigator is required to change to the new standards for collecting data and use the new Inclusion Enrollment Report format for reporting data to NIH. In some cases, this will mean that principal investigators will need to re-ask study participants about their race and ethnicity using the new two-question format. Note: principal investigators should not ask again about race and ethnicity if the subjects are no longer participating in the study.

Old Inclusion Table (4/98 Version) MS Word or PDF

- Studies begun prior to January 10, 2002 (and now in their non-competing Type 5 period) that were structured with one question about race and ethnicity may continue to report enrollment/accrual data to NIH based on the old form, i.e., using five categories of race/ethnicity. However, when they come in for competitive renewal (Type 2), they will need to change to the new standards/new form for any additional data collection.

- Principal investigators should not switch to the new form if only one question about race and ethnicity is used in data collection.

- Sample of old Inclusion Table format: http://grants.nih.gov/grants/funding/women_min/InclusionOld_Form.pdf

Investigators who have questions about these choices should contact NIH program staff for advice.

Guidance and Additional Instructions

After you have completed the Inclusion of Women and Minorities section, proceed to Inclusion of Children.

INCLUSION OF CHILDREN

- Create a section entitled “Inclusion of Children” and place it immediately following the last entry in the Inclusion of Women and Minorities section.
- 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, then you must present an acceptable justification (see below) for the exclusion.
- 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 dealing 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 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 in the “Human Subjects Research and Protection from Risks” subheading.

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 can be fully justified:

1. The research topic to be studied is not relevant to children.
2. There are laws or regulations barring 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 Director.

Guidance and Additional Instructions

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

See Policy on Inclusion of Children.

SCENARIO A: NO HUMAN SUBJECT RESEARCH PROPOSED

Criterion

If you are uncertain as to whether your research involves Human Subjects please read: Question 1: Does your proposed research involve human subjects?

Instructions

Check the box marked “No” on the Face Page (item 4).

In your application narrative, create a heading labeled “e. Human Subjects Research” and place it immediately after the last entry in the Research Design and Methods section. Include the following statement below the heading: “No Human Subjects Research is proposed in this application.”

If your research involves human specimens, cell lines and/or data from subjects, please provide a justification for your claim that no human subjects are involved.

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

Guidance and Additional Instructions

The material that you provide will be used by reviewers as part of their evaluations on the research design and methods of your proposed research.

Do not follow the instructions for Scenario A if research activities involving human subjects are planned at any time during the proposed project period, either at the applicant organization or at any other performance site or collaborating institution. You will need to consider an alternative scenario.

If you need to consider an alternative scenario return to the PHS 398 Instructions Decision Table for Section e.

or

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

SCENARIO B: HUMAN SUBJECTS RESEARCH CLAIMING EXEMPTION 4

Criteria	
Human Subjects Research	Yes
Exemption	4
Clinical Research	No
Clinical Trial	N/A
NIH-Defined Phase III Clinical Trial	N/A

Instructions and Required Information

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

Check the box marked "Yes" on the Face Page (item 4). 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 performance site or collaborating institution. "Yes" should be checked even if the research is exempt from requirements in the Federal regulations for the protection of human subjects (45 CFR Part 46).

Indicate that you are claiming Exemption 4 on the Face Page (item 4a) and enter "NA" for item 4b, since no assurance is needed.

In your application narrative, create a heading entitled "e. Human Subjects Research" and place it immediately after the last entry in the Research Design and Methods section. Include the following statement below the heading: "This Human Subjects Research falls under Exemption 4."

Address the following three items in this new section:

1. Human Subjects Involvement and Characteristics:

a. Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section.

b. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. If the characteristics of the population are not available, then the applicant should indicate that the information is unknown.

c. Identify the criteria for inclusion or exclusion of any subpopulation.

d. Explain the rationale for the involvement of vulnerable populations, such as fetuses, neonates, pregnant women, children, institutionalized individuals, or others who may be considered vulnerable populations. Exemptions 1-6 do not apply to research involving prisoners or subjects who become prisoners (see 45 CFR Part 46 Subpart C). Although Exemptions 1 and 3-6 apply to research involving children (see 45 CFR Part 46 Subpart D), Exemption 2 can only be used for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

e. List any collaborating sites where human subjects research will be performed and describe the role of those sites in performing the proposed research.

2. Sources of Materials:

a. Describe the research material obtained from living human subjects in the form of specimens, records, or data.

b. Describe any data that will be recorded on the human subjects involved in the project.

c. Describe the linkages to subjects, and indicate who will have access to subject identities.

d. Provide information about when the specimens, records, or data were collected and whether new material or data will need to be collected specifically for your proposed research project.

3. Justification:

a. Indicate that you are claiming Exemption 4.

b. Provide a justification for why your research meets the criteria for Exemption 4. Note: Even if your research is appropriate for Exemption 4, you are required to address the inclusion of children, if known.

Guidance and Additional Instructions

The material that you provide will be used by reviewers as part of their evaluations on the research design and methods of your proposed research.

What types of research meet the criteria for 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. Determining the appropriateness of Exemption 4 for research using specimens and data can be complex.

Note: Prospective collection of additional specimens does not meet the criteria for Exemption 4.

If you are uncertain as to whether your research meets the criteria for Exemption 4, refer to Exemption 4 Guidance and Information.

If you need to consider an alternative scenario, return to the PHS 398 Instructions Decision Table for Section e.

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

SCENARIO C: HUMAN SUBJECTS RESEARCH CLAIMING EXEMPTION 1, 2, 3, 5, OR 6

Criteria	
Human Subjects Research	Yes
Exemption Claimed	1, 2, 3, 5, 6
Clinical Research	Yes
Clinical Trial	N/A
NIH-Defined Phase III Clinical Trial	N/A

Instructions and Required Information

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

Check the box marked "Yes" for item 4 on the Face Page, check the box marked "Yes" for item 4a on the Face Page, enter the exemption number that you are claiming. Enter "NA" for item 4b, since no OHRP assurance number is needed for exempt research.

Although your research may be exempt from the IRB oversight provisions, it is still human subjects research, and you need to follow the instructions that are identified for each of the following topics and provide the information that is requested.

In your application narrative, create a heading entitled "e. Human Subjects Research" and place it immediately after the last entry in the Research Design and Methods section. Address the following items in this new section. Include the following statement below the heading: "This Human Subjects Research falls under Exemption(s) … ."

1. Human Subjects Involvement and Characteristics:

a. Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section.

b. Describe the characteristics of the subject population, including their anticipated number, age range, and health status.

c. Identify the criteria for inclusion or exclusion of any subpopulation (e.g., men, women, children).

d. Explain the rationale for the involvement of vulnerable populations, such as fetuses, neonates, pregnant women, children, institutionalized individuals. Please note that research involving prisoners is not exempt under any category (see 45 CFR Part 46 Subpart C).

e. List any collaborating sites where human subjects research will be performed and describe the role of those sites in performing the proposed research.

2. Sources of Materials:

a. Describe the sources of the research material obtained from living human subjects in the form of specimens, records, or data.

b. Describe any data that will be recorded on the human subjects involved in the project.

c. Describe the linkages to subjects and indicate who will have access to subject identities.

d. Provide information about when the specimens, records, or data were collected and whether new material or data will need to be collected specifically for your proposed research project.

3. Justification:

In this section, identify which exemption (1, 2, 3, 5, or 6) you are claiming. (If you are claiming Exemption 4 please refer to Scenario B and the appropriate instructions.) Justify why your research is appropriate for the exemption that you have claimed.

4. Inclusion of Women and Minorities (click and follow instructions)

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.

Create a section entitled "Inclusion of Women and Minorities" and place it immediately following the last entry in the "Human Subjects Research" section.

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.

Include the Targeted/Planned Enrollment Table (MS Word or PDF) here.

5. Inclusion of Children (click and follow instructions)

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.)

Guidance and Additional Instructions

The material that you provide will be used by reviewers as part of their evaluations on the research design and methods of your proposed research.

If you are uncertain as to whether your research meets the criteria for an exemption please read: Question 2: Is your proposed research described by one or more of the exemptions in the HHS regulations?

If you need to consider an alternative Scenario, return to the PHS 398 Instructions Decision Table for Section e.

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

SCENARIO D: CLINICAL RESEARCH

Criteria	
Human Subjects Research	Yes
Exemption	No
Clinical Research	Yes
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.

Check the box marked "Yes" for item 4 on the Face Page, for item 4a check the box marked "No," and for item 4b enter your OHRP assurance number in the space provided on the Face Page.

In your application narrative, create a section entitled "e. Human Subjects Research" immediately following the last entry in the Research Design and Methods section. Include the following statement below the heading: "This Human Subjects Research meets the definition of 'Clinical Research.'"

Create a subheading for each of the following items, follow the instructions that are identified for each topic, and provide the information that is requested:

1. **Human Subjects Research and Protection from Risks** (click and follow instructions)
2. **Inclusion of Women and Minorities** (click and follow instructions)
   Targeted/Planned Enrollment Table (MS Word or PDF)
3. **Inclusion of Children** (click and follow instructions)

If your application involves collaborating sites, provide the information identified above for each participating site.

Guidance and Additional Instructions

Research that meets the criteria for Exemption 4 is not considered clinical research.

Research that uses **existing (archived)** specimens that **can** be linked to living individuals must address the inclusion of women, minorities and children as identified above, unless the investigator does not have access to the information. The material that you provide will be used by reviewers as part of their evaluations on the research design and methods of your proposed research.

If you are uncertain as to whether your research meets the criteria for clinical research, read: Question 3: Does your proposed research include Clinical Research?

If you need to consider an alternative scenario, return to the PHS 398 Instructions Decision Table for Section e.

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

SCENARIO E. CLINICAL TRIALS

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

Instructions and Required Information

Check the box marked “Yes” for item 4 on the Face Page, for item 4a check the box marked “No,” and for item 4b enter your OHRP assurance number in the space provided.

In your application narrative, create a section entitled “e. Human Subjects Research” immediately following the last entry in the Research Design and Methods section. Include the following statement below the heading: “This Human Subjects Research meets the definition of a clinical trial.” Create a subheading for each of the following items, follow the instructions that are identified for each topic, and provide the information that is requested:

1. **Human Subjects Research and Protection from Risks** (click and follow instructions)
2. **Data and Safety Monitoring Plan** (click and follow instructions)
3. **Inclusion of Women and Minorities** (click and follow instructions)
   Targeted/Planned Enrollment Table (MS Word or PDF)
4. **Inclusion of Children** (click and follow instructions)

If your application involves collaborating sites, provide information for each of the issues identified above for each participating site.

Guidance and Additional Instructions

The material that you provide will be used by reviewers as part of their evaluations on the research design and methods of your proposed research. If you are uncertain as to whether your research includes a clinical trial please read: Question 4: Does your proposed research include a clinical trial?

If you need to consider an alternative scenario, return to the PHS 398 Instructions Decision Table for Section e.

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

SCENARIO F. NIH DEFINED PHASE III CLINICAL TRIAL

Criteria

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

Instructions and Required Information

Check the box marked “Yes” for item 4 on the Face Page, for item 4a check the box marked “No,” and for item 4b enter your OHRP assurance number in the space provided.

In your application narrative, create a section entitled “e. Human Subjects Research” immediately following the last entry in the Research Design and Methods section. Include the following statement below the heading: ”This Human Subjects Research is an NIH-Defined Phase III Clinical Trial.”

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

1. **Human Subjects Research and Protection from Risk** (click and follow instructions)
2. **Data and Safety Monitoring Plan** (click and follow instructions)
3. **Inclusion of Women and Minorities** (click and follow instructions)
   Targeted/Planned Enrollment Table (MS Word or PDF)
4. **Inclusion of Children** (click and follow instructions)

If your application involves collaborating sites, provide the information identified above for each participating site.

Guidance and Additional Instructions

The material that you provide will be used by reviewers as part of their evaluations on the research design and methods of your proposed research. If you are uncertain as to whether your research includes clinical research, read Question 5: Does your proposed research meet criteria for an NIH-Defined Phase III Clinical Trial?

If you need to consider an alternative scenario, return to the PHS 398 Instructions Decision Table for Section e.

After you have completed this section of the application, proceed to Section f. Vertebrate Animals in the PHS 398 instructions.

HUMAN SUBJECTS RESEARCH DEFINITIONS

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 and 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: **(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. For the purpose of the Guidelines 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.

Data and Safety Monitoring Plan. NIH requires a data and safety monitoring plan for each clinical trial 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.**

Gender. Refers to the classification of research subjects into either or both of two categories: women and men. 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 Subject. A living individual about whom an investigator (whether professional or student) obtains for research purposes (1) data through intervention or interaction with the individual, or (2) identifiable private information. The regulations governing the inclusion of human subjects in research extend to the use of human organs, tissues, and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects.

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. Interaction includes communication or interpersonal contact between investigator and subject.

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.

The use of autopsy materials is governed by applicable state and local law and is not directly regulated by 45 CFR Part 46.

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.

HUMAN SUBJECTS RESEARCH POLICY

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

Protection of Human Subjects

The Department of Health and Human Services (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 an applicant 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 applicant organizations proposing to involve human subjects in nonexempt research, file a written Assurance of Compliance with the Office for Human Research Protections (OHRP), establishing 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 20852 or by contacting OHRP at ohrp@osophs.dhhs.gov; Telephone: 1-866-447-4777 or (301) 496-7005.

Under DHHS regulations to protect human subjects from research risks, 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 the return of the application without review. 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.

No non-exempt research involving human subjects can be conducted under a DHHS award unless that organization is operating in accord with an approved Assurance of Compliance and provides verification that an Institutional Review Board (IRB) that is registered under the specific Assurance 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.

The Center of Biologics Evaluation and Research (CBER), FDA, regulates the use of biological products in humans at the investigational and marketing phases, including somatic cell therapies and gene transfer research. If your work involves these areas or preclinical research that will support later work in these areas, please see the Office of Recombinant DNA Activities website at http://www4.od.nih.gov/oba/.

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 the collection or study of existing data, documents, records, pathological specimens, diagnostic specimens, or tissues that are individually identifiable is considered “research involving human subjects.” The NIH has developed a user-friendly brochure to help investigators understand how the human subjects regulations 45 CFR Part 46 apply to their research. You may download this brochure, entitled "Research on Human Specimens: Are You Conducting Research Using Human Subjects?" from http://www.cancerdiagnosis.nci.nih.gov/specimens/brochure.html.

The DHHS regulations also require “Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency” (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.

Vulnerable Populations

Investigators who conduct research involving pregnant women, human fetuses and neonates, prisoners, or children must follow the provisions of the regulations in Subparts B, C, and D of 45 CFR Part 46, respectively, which describe the additional protections required for these 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. Relevant information may be obtained at the OHRP website (http://www.hhs.gov/ohrp/policy/index.html).

REMINDER: HHS regulations at 45 CFR Part 46, subpart C describe requirements for additional protections for research involving prisoners as subjects or individuals who become prisoners after the research has started. Refer to: http://www.hhs.gov/ohrp/humansubjects/guidance/prisoner.htm for complete instructions.

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 observations of public behavior when the investigator(s) do not participate in the activities being observed.

Data and Safety Monitoring Plans for Clinical Trials

NIH requires a data and safety monitoring plan for each clinical trial 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. 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.

Research on Transplantation of Human Fetal Tissue

In signing the application Face Page, the duly authorized 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.

Research Using Human Embryonic Stem Cells

http://stemcells.nih.gov/index.asp

In signing the application Face Page, the duly authorized representative of the applicant organization certifies that if research using human embryonic stem cells is proposed, the applicant organization will be in compliance with the "Notice of Extended Receipt Date and Supplemental Information Guidance for Applications Requesting Funding that Proposes Research with Human Embryonic Stem Cells" (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-006.html).

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 OHRP-registered IRB. See http://www.hhs.gov/ohrp/ to register an IRB. Documentation of IRB approval must be sent to the Grants Management Office identified in the notice requesting certification. This IRB certification must include: the PHS application number, title of the project, name of the principal investigator/program director, date of IRB approval, and appropriate signatures.

An institution is automatically considered to be engaged in human subjects research when it receives an NIH award to support nonexempt human subjects research. 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.

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

If 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.

Required Education in the Protection of Human Research Participants

NIH requires education on the protection of human research participants for all individuals identified as Key Personnel before funds are awarded for applications or contract proposals involving human subjects. For information relating to this requirement, see the following 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 found 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 Key Personnel involved in human subjects research. Although NIH does not endorse programs, there are curricula available that can provide guidance or that can be modified to provide training in this area. See http://ohsr.od.nih.gov/ 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.

Relevant Policies and Information

PROCEDURES FOR SUBMISSION OF COMPLIANCE DOCUMENTS TO THE HUMAN PLURIPOTENT STEM CELL REVIEW GROUP FOR THE RESEARCH USE OF HUMAN EMBRYONIC GERM CELLS	NOTICE: NOT-OD-02-049 http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html
GUIDANCE FOR INVESTIGATORS AND INSTITUTIONAL REVIEW BOARDS REGARDING RESEARCH INVOLVING HUMAN EMBRYONIC STEM CELLS, GERM CELLS AND STEM CELL-DERIVED TEST ARTICLES	NOTICE: NOT-OD-02-044 http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-044.html
IMPLEMENTATION ISSUES FOR HUMAN EMBRYONIC STEM CELL RESEARCH - FREQUENTLY ASKED QUESTIONS	NOTICE: NOT-OD-02-014 http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-014.html
FEDERAL GOVERNMENT CLEARANCES FOR RECEIPT OF INTERNATIONAL SHIPMENT OF HUMAN EMBRYONIC STEM CELLS	NOTICE: NOT-OD-02-013 http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-013.html
NOTICE OF EXTENDED RECEIPT DATE AND SUPPLEMENTAL INFORMATION GUIDANCE FOR APPLICATIONS REQUESTING FUNDING THAT PROPOSES RESEARCH WITH HUMAN EMBRYONIC STEM CELLS	NOTICE: NOT-OD-02-006 http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-006.html
NOTICE OF CRITERIA FOR FEDERAL FUNDING OF RESEARCH ON EXISTING HUMAN EMBRYONIC STEM CELLS AND ESTABLISHMENT OF NIH HUMAN EMBRYONIC STEM CELL REGISTRY	NOTICE: NOT-OD-02-005 http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html
NIH FUNDING OF RESEARCH USING SPECIFIED EXISTING HUMAN EMBRYONIC STEM CELLS	NOTICE: NOT-OD-01-058 http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-01-059.html

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

It is the policy of NIH 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 Institute/Center 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 Institute/Center 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.

NIH Policy on Inclusion of Children

(See Definition of "child".)

Research involving children must comply with the NIH Policy and Guidelines on the Inclusion of Children in Clinical Research. The following excerpts provide the key policy statements. Investigators should obtain full copies of the Policy and Guidelines from NIH staff, or from the NIH grants Web site under 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.

In addition, 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.

Additionally, 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.

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

The Office of Management and Budget (OMB) (http://www.whitehouse.gov/omb/fedreg/ombdir15.html) defines minimum standards for maintaining, collecting and presenting data on race and ethnicity for all Federal reporting agencies (including NIH). The categories in this classification are social-political constructs and should not be interpreted as being anthropological in nature. The standards were revised in 1997 and now include two ethnic categories, "Hispanic or Latino" and "Not Hispanic or Latino." There are 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. 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. (http://grants2.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm).

Guidance on Collecting Race and Ethnicity Data from Study 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. An example of a format for collecting information from study subjects in the US and that meets the OMB requirements can be found in the Ethnic Origin and Race section of the Personal Data Form Page (MS Word or PDF) in the PHS 398.

See NIH Policy on Inclusion of Women and Minorities.

Collecting Data on Foreign Populations: If you are conducting clinical research outside of the US, you should design culturally sensitive and appropriate data collection items and instruments that allow subjects to self-identify their ethnic and racial affiliation in a culturally appropriate manner. These items, however, should be designed in a way that allow you, the investigator, to aggregate the information into the OMB minimally required ethnic and racial categories when reporting the information to NIH.

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. Under these circumstances, investigators are not required to re-contact subjects solely to comply with the newly revised categories. If the existing data on ethnicity and race allow accurate correspondence with the new categories, the investigator can use the format in the Targeted/Planned Enrollment table (MS Word or PDF). However, if the existing data do not allow accurate correspondence with the new categories, information may be reported using the former categories and according to the format in the 4/98 Version of the Inclusion Table http://grants.nih.gov/grants/funding/women_min/InclusionOld_Form.pdf.

Annual Progress Reports (Type 5 applications) and Competing Supplement Applications

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 EITHER the new Inclusion Enrollment Report (MS Word or PDF) OR the format in the former 4/98 Version of the Inclusion Table (MS Word or PDF).

For competing supplement applications, any proposed additions to the Targeted/Planned Enrollment Table should be provided, in addition to the current Inclusion Enrollment Table.

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

Investigators may choose to report ethnicity/race and sex/gender sample composition using EITHER the new Inclusion Enrollment Report (MS Word or PDF) OR the format in the former 4/98 Version of the Inclusion Table (MS Word or PDF).

[Note: If investigators with on-going data collection choose to report information using the new Inclusion Enrollment Report, they must continue to use this format for the remaining years of the project.]

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

Investigators may EITHER continue to report using the former categories and according to the 4/98 Version of the Inclusion Table, OR, if data allow accurate correspondence with the new categories, use the format in the new Inclusion Enrollment Report.

Additional Information

Additional information on NIH policy regarding the Inclusion of Women and Minorities in Clinical Research can be found at the website http://grants.nih.gov/grants/funding/women_min/women_min.htm.