

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

Scenario A. No Human Subjects Research Proposed

Criteria

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

Instructions and Required Information

If proposed studies using human data or biological specimens do not involve human subjects as described in the OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (<http://www.hhs.gov/ohrp/policy/cdebiol.html>), provide an explanation of why the proposed studies do not constitute research involving human subjects. Save this explanation as a .pdf file entitled “Human Subjects Research.pdf” and attach in line 6 of the PHS 398 Research Plan (for K applicants, line 14 of the PHS 398 Career Development Award Supplemental Form).

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

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

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

Scenario B. Non-Exempt Human Subjects Research

Criteria

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

Instructions and Required Information

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

In the application narrative, provide the required information for each of the following topics below as a separate file. Save each of the four files as a .pdf file and attach in lines 6-9 of the PHS 398 Research Plan (for K applicants, lines 14-17 of the PHS 398 Career Development Award Supplemental Form).

Protections of Human Subjects - [Section 4.1 - 4.1.4](#)

Inclusion of Women and Minorities - [Section 4.2](#)

Targeted/Planned Enrollment Table(s) - [Section 4.3](#)

Inclusion of Children - [Section 4.4](#)

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

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

Criteria

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

Instructions and Required Information

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

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

In the application narrative, provide the required information for each of the following topics below as a separate files. Save each of the four files as a .pdf file and attach in lines 6-9 of the PHS 398 Research Plan (for K applicants, lines 14-17 of the PHS 398 Career Development Award Supplemental Form).

Protections for Human Subjects – Include the following statement: ‘This Human Subjects Research falls under Exemption(s)’ Clearly identify which exemption(s) (1, 2, 3, 4*, 5, 6) you are claiming, and justify why the research meets the criteria for exemption that you have claimed. If the research will include a clinical trial, even if exempt, include a Data and Safety Monitoring Plan – [Section 4.1.5](#), and address the ClinicalTrials.gov requirements if applicable – [Section 4.1.6](#).

Inclusion of Women and Minorities - [Section 4.2](#)

Targeted/Planned Enrollment Table(s) - [Section 4.3](#)

Inclusion of Children - [Section 4.4](#)

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

Scenario D: Delayed-Onset Human Subjects Research

Criteria

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

Instructions and Required Information

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

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

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

Under no circumstance may human subjects be involved in research until approval is granted by the awarding entity, and certification of IRB approval has been accepted by the agency.

In the application narrative, provide the required information for each of the following topics below as a separate file. Save each of the four files as a .pdf file and attach in lines 6-9 of the PHS 398 Research Plan (for K applicants, lines 14-17 of the PHS 398 Career Development Award Supplemental Form). Follow the instructions that are identified for each of the following topics and EITHER provide as much of the information that is requested as possible; OR describe why it is not possible to provide the information due to delayed-onset of human subjects research:

Protection of Human Subjects - [Section 4.1](#). If the research will include a clinical trial, even if exempt, include a Data and Safety Monitoring Plan as described in [Section 4.1.5](#), and address the ClinicalTrials.gov requirements if applicable – [Section 4.1.6](#).

Inclusion of Women and Minorities - [Section 4.2](#)

Targeted/Planned Enrollment Table(s) - [Section 4.3](#)

Inclusion of Children - [Section 4.4](#)

Scenario E: Clinical Trial

Criteria

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

Instructions and Required Information

In the application narrative, provide the required information for each of the following topics below as a separate file. Save each of the four files as a .pdf file and attach in lines 6-9 of the PHS 398 Research Plan (for K applicants, lines 14-17 of the PHS 398 Career Development Award Supplemental Form).

Protection of Human Subjects - [Section 4.1 - 4.1.6](#)

Inclusion of Women and Minorities - [Section 4.2](#)

Targeted/Planned Enrollment Table(s) - [Section 4.3](#)

Inclusion of Children - [Section 4.4](#)

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

Scenario F: NIH Defined Phase III Clinical Trial

Criteria

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

Instructions and Required Information

In the application narrative, provide the required information for each of the following topics below as a separate file. Save each of the four files as a .pdf file and attach in lines 6-9 of the PHS 398 Research Plan (for K applicants, lines 14-17 of the PHS 398 Career Development Award Supplemental Form).

Protection of Human Subjects - [Section 4.1 - 4.1.6](#). Also include the statement that 'This Human Subjects Research involves an NIH-Defined Phase III Clinical Trial.'

Inclusion of Women and Minorities - [Section 4.2 - 4.2.1](#)

Targeted/Planned Enrollment Table(s) - [Section 4.3](#)

Inclusion of Children - [Section 4.4](#)

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

4. Instructions Pertaining to Non-Exempt Human Subjects Research

In your PHS 398 Research Plan Component, include attachments for Items 6 through 9, if required. Although no specific page limitation applies to this section of the application, be succinct. Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the protection of human subjects. DHHS regulations and policies governing human subjects research are described and referenced in Section 5 below. Use subheadings to address the issues listed under items 4.1-4.4 below. If your research includes a clinical trial, include a subheading "Data and Safety Monitoring Plan" and follow the instructions in 4.2 below. If your research includes an NIH-Defined Phase III Clinical Trial, follow the additional instructions in 4.2.1 below.

4.1 Protection of Human Subjects

4.1.1 Risks to Human Subjects

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

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

b. *Sources of Materials*

- Describe the research material obtained from living individuals in the form of specimens, records, or data.
- Describe any data that will be collected from human subjects for the project(s) described in the application.

- Indicate who will have access to individually identifiable private information about human subjects.
 - Provide information about how the specimens, records, and/or data are collected, managed, and protected as well as whether material or data that include individually identifiable private information will be collected specifically for the proposed research project.
- c. **Potential Risks**
- Describe the potential risks to subjects (physical, psychological, financial, legal, or other), and assess their likelihood and seriousness to the human subjects.
 - Where appropriate, describe alternative treatments and procedures, including the risks and potential benefits of the alternative treatments and procedures, to participants in the proposed research.

4.1.2 Adequacy of Protection Against Risks

a. **Recruitment and Informed Consent**

- Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.
- Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver. Informed consent document(s) need not be submitted to the PHS agencies unless requested.

b. **Protections Against Risk**

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

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

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

4.1.4 Importance of the Knowledge to be Gained

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

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

4.1.5 Data and Safety Monitoring Plan

The NIH Data and Safety Monitoring Plan Policy is described and referenced in [Section 5.3](#).

- If the proposed research includes a clinical trial, create a heading entitled "Data and Safety Monitoring Plan."
- Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring. Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the Institutional Review Board (IRB), the funding I/C, the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA) in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations. Be succinct. Contact the FDA (<http://www.fda.gov/>) and also see the following Web sites for more information related to IND and IDE requirements:
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr312_01.html (IND)
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr812_01.html (IDE)
- The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:
 - a. PD/PI (required)
 - b. Institutional Review Board (IRB) (required)
 - c. Independent individual/safety officer
 - d. Designated medical monitor
 - e. Internal Committee or Board with explicit guidelines

- f. Data and Safety Monitoring Board (DSMB). NIH specifically requires the establishment of Data and Safety Monitoring Boards (DSMBs) for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally for Phase III clinical trials. Although Phase I and Phase II clinical trials may also need DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.
- A detailed Data and Safety Monitoring Plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects. For additional guidance on creating this Plan, see <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>.

4.1.6 ClinicalTrials.gov Requirements

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

NIH encourages registration of ALL clinical trials whether required under the law or not.

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

The NIH implementation of FDAAA requires:

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

For **competing** (new and renewal) applications that include applicable clinical trials which require registration and, **in certain cases, require** results reporting under FDAAA, provide the NCT number/s, Brief Title/s (protocol title intended for the lay public – see [Definitions](#)), and the identity (name, organization) **of the responsible party and their contact information** (e-mail address is required for internal administrative use only) in the human subjects section of the Research Plan under a section heading entitled ClinicalTrials.gov. If a new applicable clinical trial is proposed, **or if the grant will support an applicable clinical trial that is ongoing but not yet required to register under FDAAA (e.g. less than 21 days have passed since enrollment of the first patient), the human subjects section of the Research Plan must include a clear statement**, under the heading ClinicalTrials.gov, that the **project** includes an applicable clinical trial which will require registration in ClinicalTrials.gov.

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

(1) the sponsor of the clinical trial (as defined in 21 CFR 50.3)

(<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=50.3>), or

(2) the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee (provided that “the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements” for submitting information under the law)

([http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf)

[docid=f:publ085.110.pdf](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf)). See PL 110-85, Section 801(a), (adding new 42 U.S.C. 282(j)(1)(A)(ix)).

For the complete statutory definitions of “responsible party” and “applicable clinical trial”, refer to [Elaboration of Definitions of Responsible Party and Applicable Clinical Trial](#).

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

Additional information can be found on the ClinicalTrials.gov Web site

(http://grants.nih.gov/ClinicalTrials_fdaaa).

4.2 Inclusion of Women and Minorities

In the attachment for Item 7, include a heading entitled “Inclusion of Women and Minorities.” Although no specific page limitation applies to this section of the application, be succinct. The NIH Policy on the Inclusion of Women and Minorities in Clinical Research is described and referenced in [Section 5.6](#).

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

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

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

Below are examples of acceptable justifications for the exclusion of:

A. One gender:

1. One gender is excluded from the study because:

- inclusion of these individuals would be inappropriate with respect to their health;
 - the research question addressed is relevant to only one gender;
 - evidence from prior research strongly demonstrates no difference between genders; or
 - sufficient data already exist with regard to the outcome of comparable studies in the excluded gender, and duplication is not needed in this study.
2. One gender is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; very small numbers of subjects are involved; or overriding factors dictate selection of subjects, such as matching of transplant recipients, or availability of rare surgical specimens).
 3. Gender representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or data-sets with incomplete gender documentation are used), and this does not compromise the scientific objectives of the research.

B. Minority groups or subgroups:

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

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

If the proposed research includes an [NIH-Defined Phase III Clinical Trial](#), the section on Inclusion of Women and Minorities also must address whether clinically important sex/gender and/or race/ethnicity differences are expected from the intervention effect. The discussion may include supporting evidence and/or data derived from animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies, and observational, natural history, epidemiology and other relevant studies. The discussion of expected sex/gender and/or race/ethnicity differences in intervention effect must include selection and discussion of one of the following analysis plans:

- Plans to conduct valid analyses to detect significant differences in intervention effect among sex/gender and/or racial/ethnic subgroups when prior studies strongly support these significant differences among subgroups, *or*
- Plans to include and analyze sex/gender and/or racial/ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups. (Representation of sex/gender and racial/ethnic groups is not required as subject selection criteria, but inclusion is encouraged.), *or*
- Plans to conduct valid analyses of the intervention effect in sex/gender and/or racial/ethnic subgroups (without requiring high statistical power for each subgroup) when the prior studies neither support nor negate significant differences in intervention effect among subgroups.

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

If your application includes Targeted/Planned Enrollment tables, save all as a single PDF file and attach them using section 8. Targeted/Planned Enrollment of the PHS 398 Research Plan Component.

The NIH Policy on Reporting Race and Ethnicity Data for Subjects in Clinical Research is described and referenced in [Section 5.8](#).

A. New Applications

All new clinical research studies should collect and report information on participants with respect to two categories of ethnicity and five categories of race. The Inclusion Enrollment Report (http://grants.nih.gov/grants/funding/424/SF424R-R_enrollmentreport.doc) for reporting summary data on participants to NIH includes two categories of ethnicity and five categories of race and is based on the Office of Management and Budget (OMB) reporting standards for data on race and ethnicity. Investigators should review the instructions and Frequently Asked Questions about using the Enrollment Table format at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html>.

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

Instructions for Completing Targeted/Planned Enrollment Table

(http://grants.nih.gov/grants/funding/424/SF424R-R_enrollment.doc)

Attach the Targeted/Planned Enrollment Table as Item 8. Provide the study title. If the application involves subprojects, provide Targeted Enrollment Tables for each subproject description.

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

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

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

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

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

List any proposed racial/ethnic subpopulations below the table.

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

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

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

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

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

Investigators should use the Inclusion Enrollment Report.

Research Conducted at Foreign Sites:

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

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

B. Renewal Application and Progress Reports

The Inclusion Enrollment Report (<http://grants.nih.gov/grants/funding/424/SF424R-R-enrollmentreport.doc>) must be used for reporting accrual data to the NIH. For Revision applications, any proposed additions to the Targeted/Planned Enrollment Tables should be provided, in addition to the Inclusion Enrollment Report. In annual progress reports, investigators conducting clinical research are required to provide the cumulative total enrollment of subjects to-date, showing the distribution by ethnic/racial categories and sex/gender on the Inclusion Enrollment Report, and must update the Targeted/Planned Enrollment Table as needed.

4.4 Inclusion of Children

The NIH Policy on Inclusion of Children is referenced and described in [Section 5.7](#). Instructions for Item 9 of the Research Plan are as follows:

- Create a section entitled “Inclusion of Children” and place it immediately following the Targeted/Planned Enrollment Table.
- For the purpose of implementing these guidelines, a *child* is defined as an individual under the age of 21 years (for additional information see <http://grants.nih.gov/grants/funding/children/children.htm> and <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>).
- Provide either a description of the plans to include children, or, if children will be excluded from the proposed research, application, or proposal, present an acceptable justification for the exclusion (see below).
- If children are included, the description of the plan should include a rationale for selecting a specific age range of children. The plan also must include a description of the expertise of the investigative team for working with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.
- Scientific Review Groups will assess each application as being acceptable or unacceptable with regard to the age-appropriate inclusion or exclusion of children in the proposed research project.
- When children are involved in research, the Additional Protections for Children Involved as Subjects in Research ([45 CFR part 46 Subpart D](#)) apply and must be addressed under the Protections Against Risk subheading (4.1.2.b).

Justifications for Exclusion of Children

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

1. The research topic to be studied is not relevant to children.
2. Laws or regulations bar the inclusion of children in the research.
3. The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be needlessly redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.
4. A separate, age-specific study in children is warranted and preferable. Examples include:

- a. The condition is relatively rare in children, as compared to adults (in that extraordinary effort would be needed to include children, although in rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected to assemble a similar child population with the rare condition); or
 - b. The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
 - c. Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some instances, consideration should be given to taking these differences into account in the study design and expanding the hypotheses tested, or the interventions planned, to allow inclusion of children rather than excluding them.
5. Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). Although children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.
 6. Study designs are aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children).
 7. Other special cases can be justified by the investigator and found acceptable to the review group and the Institute/Center Director.