Human Subjects Protection and Inclusion of Women, Minorities, and Children

Guidelines for Review of NIH Applications

HUMAN SUBJECTS PROTECTION

Requirements for Review

Federal regulations for the protection of human research subjects (45 CFR 46), require that the evaluation of research applications that involve human subjects take into consideration the risk to subjects, the adequacy of protections against risk, potential benefits of the research to subjects and others, and the importance of the knowledge to be gained.

The NIH Peer Review regulations (42 C.F.R. 52h) specify that reviewers will take into account, in determining overall impact that the project in the application could have on the research field involved, the adequacy of the proposed protection for humans. Therefore, reviewers must evaluate the proposed plans to protect human subjects from research risks, as appropriate for the research proposed, as one of the review criteria that factor into the evaluation of scientific and technical merit.

In addition to federal regulations about the protection of human research subjects, NIH policies require that applications involving Clinical Trials include a data and safety monitoring plan and that NIH-defined Phase III clinical trials also describe a data and safety monitoring board. Data safety and monitoring plans must also be evaluated by peer reviewers.

Reviewer Responsibilities

— For applications involving human subjects:
- Determine if a claim for exemption is adequately justified in applications that indicate the proposed research is exempt **OR**
- Evaluate the proposed plan for the involvement of human subjects in non-exempt human subjects research applications and determine if subjects appear to be adequately protected from research risks (see Human Subjects Protection and Inclusion Worksheet).
- For applications that involve a clinical trial, determine if the plans for data and safety monitoring, including the description of a data and safety monitoring board if necessary, are adequate.

— For applications that claim no involvement of human subjects but propose the use of existing human data or biological specimens, evaluate if the justification provided about why the proposed research does not involve human subjects is acceptable.
- Rate the application as Acceptable, Unacceptable, or Not Applicable in terms of human subjects involvement and prepare written comments, including specific comments describing concerns for applications rated as Unacceptable (see Human Subjects Protection and Inclusion Worksheet).

— For applications that do not involve human subjects or the use of human data or specimens, rate the application as Not Applicable for this criterion. In this case, the Inclusion criterion, as described below, will also be Not Applicable.

INCLUSION OF WOMEN, MINORITIES, AND CHILDREN

Requirements for Review

Public Law 103-43 requires that women and minority subjects be included in all clinical research studies. Additionally, NIH policy requires that women and minorities must be included in Phase III clinical trials in numbers adequate to allow for valid analyses of gender and/or racial/ethnic differences in intervention effects. NIH policy also states that children (defined as persons under the age of 21) be included in human subjects research projects supported by NIH unless an acceptable justification for their exclusion is provided.

The NIH Peer Review regulations (42 C.F.R. 52h) specify that reviewers will take into account, in determining overall impact that the project in the application could have on the research field involved, the adequacy of plans to include both genders, minorities, children and special populations as appropriate for the scientific goals of the research. Therefore, reviewers must evaluate the proposed plans for inclusion of women, minorities and children as one of the review criteria that factor into the evaluation of scientific and technical merit.

Reviewer Responsibilities

- Evaluate whether the gender and minority characteristics of the proposed sample and the plan for the inclusion of children are scientifically acceptable given the aims of the research.
- Rate the application as Acceptable or Unacceptable with respect to the proposed inclusion of Women, Minorities and Children, assign codes, and prepare comments (see Human Subjects Protection and Inclusion Worksheet).

BACKGROUND AND REFERENCES – HUMAN SUBJECTS PROTECTION

Federal Regulations for Protection of Human Research Subjects (45 CFR 46):
http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

Definition of Human Subject: a living individual about whom an investigator (whether professional or student) conducting research obtains

1) Data through intervention or interaction with the individual, or
2) Identifiable private information.

- *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.

Research Involving Coded Private information or Biological Specimens: Research that involves only

the use of human specimens or data is not considered human subjects research if:

- All subjects are deceased **OR**
- The data/specimens were not obtained specifically for the proposed research AND none of the investigators involved in the research can ascertain the identity of the subjects, either directly or indirectly.

  See http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm for more detailed information

Human Subjects Research Exemptions (45 CFR 46.101):

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.
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.
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. (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
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.
5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which 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.
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.

Data and Safety Monitoring Plan:

For information about reviewing the Data and Safety Monitoring Plan, please visit http://grants.nih.gov/grants/policy/hs/data_safety.htm.

BACKGROUND AND REFERENCES - INCLUSION OF WOMEN, MINORITIES, AND CHILDREN

NIH Policies regarding inclusion of women and minorities:
http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

NIH Policies regarding the inclusion of children:

http://grants.nih.gov/grants/funding/children/children.htm

Definitions

Clinical research:

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.

Phase III clinical trials research:

Phase III clinical trials research is defined as broadly based, prospective clinical investigations for the purpose of investigating 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.

Gender: The classification of humans as either female or male.

Minority group: A readily identifiable subset of the U.S. population distinguished by either racial, ethnic, and/or cultural heritage. In accordance with OMB Directive No. 15, the currently defined groups are American Indian or Alaskan Native; Asian or Pacific Islander; Black, not of Hispanic origin; and Hispanic.

Children: Individuals under the age of 21 years.

Reviewer Coding

Three three digit alphanumeric codes are used to summarize reviewer's evaluation of inclusion of women, minorities, and children. The three digit code is comprised as follows.

- First digit: G, M, or C to indicate gender, minority or children, respectively
- Second digit: 1-5 to define the inclusion status
- Third digit: A or U to indicate scientific acceptability, given the stated research aims

Each application involving human subjects receives three separate alphanumeric codes, for gender, minorities, and children, respectively. A code should be assigned to each individual project or subproject in an application containing multiple projects or subprojects and involving distinct populations or specimen collections. A single overall code ALSO should be assigned to the entire application. If any project/subproject is found "Unacceptable" (U), the overall code should be U. The overall coding should reflect the representation in all projects/subprojects, even if some are single gender or involve no minorities.

Gender Inclusion Codes

G1A = Both genders, acceptable
G1U = Both genders, unacceptable
G2A = Only women, acceptable
G2U = Only women, unacceptable
G3A = Only men, acceptable
G3U = Only men, unacceptable
G4A = gender composition unknown, acceptable
G4U = gender composition unknown, unacceptable

Minority Inclusion Codes

M1A = Minority and nonminority, acceptable
M1U = Minority and nonminority, unacceptable
M2A = Only minority, acceptable
M2U = Only minority, unacceptable
M3A = Only nonminority, acceptable
M3U = Only nonminority, unacceptable
M4A = minority composition unknown, acceptable
M4U = minority composition unknown, unacceptable
M5A = only foreign subjects, acceptable
M5U = only foreign subjects, unacceptable

Children Inclusion Codes

C1A = Children and adults, acceptable
C1U = Children and adults, unacceptable
C2A = Only children, acceptable
C2U = Only children, unacceptable
C3A = No children included, acceptable
C3U = No children included, unacceptable
C4A = Representation of children unknown, acceptable
C4U = Representation of children unknown, unacceptable

It is not anticipated that every study will include both genders, all minority groups and subgroups, and children. Inclusion should be determined by the scientific questions under

examination. Applications should describe and justify fully the samples that will be included in the research.

Reviewer Comments

Reviewer Comments are required for all codes. Examples of comments follow.

- **G1U:** Gender representation is unacceptable. Although both genders are represented, there are too few members of one gender to answer the questions posed.
- **G2A:** Gender composition is scientifically acceptable, although only females are represented, because similar research already has been done or is underway using male subjects.
- **C3A:** No children included. This is acceptable as knee replacement is rare in children as compared to adults.
- **M4U:** Minority representation is unknown. The application does not provide sufficient information about the racial/ethnic composition of the study population. The application does not comply with requirements and is unacceptable.