



## **GLOSSARY OF TERMS FOR HUMAN SUBJECTS PROTECTION AND INCLUSION ISSUES**

**AMERICAN INDIAN OR ALASKA NATIVE:**

**ASIAN:**

**BLACK OR AFRICAN AMERICAN:**

**CHILD:**

**CLINICAL RESEARCH:**

**CLINICAL TRIAL:**

**EXEMPTION CATEGORIES:**

**GENDER:**

**HISPANIC OR LATINO:**

**HUMAN SUBJECTS:**

**HUMAN SUBJECTS CONCERN:**

**HUMAN SUBJECTS RISK AND PROTECTION ISSUES:**

**MAJORITY GROUP:**

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**NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER:**

**NIH-DEFINED PHASE III CLINICAL TRIAL:**

**OUTREACH STRATEGIES:**

**RACIAL AND ETHNIC CATEGORIES:**

**RESEARCH PORTFOLIO:**

**SCIENTIFICALLY ACCEPTABLE OR UNACCEPTABLE:**

**SIGNIFICANT DIFFERENCE:**

**SUBPOPULATIONS:**

**VALID ANALYSIS:**

**WHITE:**



**AMERICAN INDIAN OR ALASKA NATIVE:**

A person having origins in any of the original peoples of North, Central, or South America and maintains tribal affiliation or community

**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.

**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."

**CHILD:**

For purposes of this policy, a child is an individual under the age of 21 years. This policy and definition do not affect the human subject protection regulations for research on children [45 CFR 46](#)) and their provisions for assent which remain unchanged.

It should be noted that the definition of child described above will pertain notwithstanding the FDA definition of a child as an individual from infancy to 16 years of age, and varying definitions employed by some states. Generally, state laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. However, state laws vary, and many do not address when a child can consent to participate in research. Federal Regulations ([45 CFR 46](#), subpart D, Sec.401-409) address DHHS protections for children who participate in research, and rely on state definitions of "child" for consent purposes. Consequently, the children included in this policy (persons under the age of 21) may differ in the age at which their own consent is required and sufficient to participate in research under 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 (see also <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>).

**CLINICAL RESEARCH:**

The NIH definition of clinical research is based on the [1997 Report of the NIH Director's Panel on Clinical Research](#) that defines clinical research in the following three parts:

- (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: Autopsy material is not covered by the policy.

When the research under review is essentially a service (e.g., statistical center or analysis laboratory) in support of another activity already found to be in compliance with this policy, a second review is not necessary.



Training grants (T32, T34, T35) are exempt from coding requirements but a term or condition of award will specify that all projects to which trainees are assigned must already be in compliance with the NIH policy on inclusion of women and minorities in clinical research.

### **CLINICAL TRIAL:**

For purposes of reviewing applications submitted to the NIH, a clinical trial is operationally defined 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. Clinical trials of experimental drug, treatment, device or behavioral intervention may proceed through four phases:

#### **Phase I Clinical Trial:**

Phase I clinical trials are done to test a new biomedical or behavioral intervention in a small group of people (e.g. 20-80) for the first time to evaluate safety (e.g. determine a safe dosage range, and identify side effects).

#### **Phase II Clinical Trial:**

Phase II clinical trials are done to 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 Clinical Trial:**

Phase III studies are done to study 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 Clinical Trial:**

Phase IV studies are done 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 on the Inclusion of Women and Minorities, an NIH-defined Phase III clinical trial is a broadly based prospective NIH-defined 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 control 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.

### **EXEMPTION CATEGORIES:**

The six categories of research that qualify for exemption from coverage by the regulations include activities in which the only involvement of human subjects will be in one or more of the following six categories:

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**Exemption 1: Instructional strategies in established educational settings**

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

**Exemption 2: Educational tests unlinkable to individuals and no risks from disclosure**

Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (a) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (b) 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 3: Educational tests on public officials, or absolute federally mandated confidentiality**

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 (2)(b) of this section, if: (a) the human subjects are elected or appointed public officials or candidates for public office; or (b) 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: Existing data/specimens, publicly available, unlinkable to individuals**

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.

**Exemption 5: Demonstration projects concerning public benefit or service programs**

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: (a) public benefit or service programs; (b) procedures for obtaining benefits or services under those programs; (c) possible changes in or alternatives to those programs or procedures; or (d) possible changes in methods or levels of payment for benefits or services under those programs.

**Exemption 6: Taste and quality evaluation of foods without additives exceeding regulated levels**

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

**GENDER:**

Refers to the classification of research subjects into either or both of two categories: 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).



### **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".

### **HUMAN SUBJECTS:**

The CODE OF FEDERAL REGULATIONS, TITLE 45, PART 46, PROTECTION OF HUMAN SUBJECTS ([45CFR46](#)) defines human subjects as follows:

Human subject means 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 (see also the [decision charts](#) provided by the [Office of Human Research Protection](#) ).

In addition, legal requirements 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. Legal obligations to protect human subjects apply, for example, to research that uses—

Bodily materials, such as cells, blood or urine, tissues, organs, hair or nail clippings, even if you did not collect these materials

Residual diagnostic specimens, 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 individuals, even if the information was not specifically collected for the study in question.

Research on cell lines or DNA samples that can be associated with individuals falls into this category.

### **HUMAN SUBJECTS CONCERN:**

A human subject concern is defined as any actual or potential unacceptable risk, or inadequate protection against risk, to human subjects as described in any portion of the application.

### **HUMAN SUBJECTS RISK AND PROTECTION ISSUES:**

The PHS 398 application instructions require that applicants address the following items in the Research Plan – Section e of their applications:

#### **1. Subjects Involvement and Characteristics.**

Provide a detailed description of the proposed involvement of human subjects in the work previously 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, pregnant women, children, prisoners, institutionalized individuals, or others who are likely to be vulnerable populations.

## **2. Sources of Materials.**

Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

## **3. Recruitment and Informed Consent.**

Describe plans for the recruitment of subjects and the consent procedures to be followed. Include 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. The informed consent document should be submitted to the PHS only if requested.

## **4. Potential Risks.**

Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects. Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, where appropriate, describe the provisions for monitoring the data collection to ensure the safety of subjects.

## **5. Protection Against Risk.**

Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects.

## **6. Benefits.**

Discuss the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.

### **MAJORITY GROUP:**

White, not of Hispanic Origin: A person having origins in any of the original peoples of Europe, North Africa, or the Middle East.

NIH recognizes the diversity of the U.S. population and that changing demographics are reflected in the changing racial and ethnic composition of the population. The terms "minority groups" and "minority subpopulations" are meant to be inclusive, rather than exclusive, of differing racial and ethnic categories.

### **MINORITY GROUPS:**

A minority group is a readily identifiable subset of the U.S. population, which is distinguished by racial, ethnic, and/or cultural heritage.



It is not anticipated that every study will include all minority groups and subgroups. The inclusion of minority groups should be determined by the scientific questions under examination and their relevance to racial or ethnic groups.

Applicants should describe the subgroups to be included in the research. In foreign research projects involving human subjects, the definition of minority groups may be different than in the US.

**NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER:**

A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

**NIH-DEFINED PHASE III CLINICAL TRIAL:**

For the purpose of the Guidelines on the Inclusion of Women and Minorities, an NIH-defined Phase III clinical trial is a broadly based prospective NIH-defined 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 control 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.

**OUTREACH STRATEGIES:**

These are outreach efforts by investigators and their staff(s) to appropriately recruit and retain populations of interest into research studies. Such efforts should represent a thoughtful and culturally sensitive plan of outreach and generally include involvement of other individuals and organizations relevant to the populations and communities of interest, e.g., family, religious organizations, community leaders and informal gatekeepers, and public and private institutions and organizations. The objective is to establish appropriate lines of communication and cooperation to build mutual trust and cooperation such that both the study and the participants benefit from such collaboration.

**RACIAL AND ETHNIC CATEGORIES:**

The Office of Management and Budget (OMB) Directive No. 15 defines the minimum standard of basic racial and ethnic categories, which are used by NIH. These definitions are used because they allow comparisons to many national databases, especially national health databases. Therefore, the racial and ethnic categories described in this document should be used as basic guidance, cognizant of the distinction based on cultural heritage.

**RESEARCH PORTFOLIO:**

Each Institute and Center at the NIH has its own research portfolio, i.e., its "holdings" in research grants, cooperative agreements, contracts and intramural studies. The Institute or Center evaluates the research awards in its portfolio to identify those areas where there are knowledge gaps or which need special attention to advance the science involved. NIH may consider funding projects to achieve a research portfolio reflecting diverse study populations. With the implementation of this new policy, there will be a need to ensure that sufficient resources are provided within a program to allow for data to be developed for a smooth transition from basic research to NIH-defined Phase III clinical trials that meet policy requirements.





### **SCIENTIFICALLY ACCEPTABLE OR UNACCEPTABLE:**

A determination, based on whether or not the gender or minority representation proposed in the research protocol conforms with NIH policy guidelines pertinent to the scientific purpose and type of study. A determination of unacceptable is reflected in the priority score assigned to the application. In addition, the definition of what constitutes SCIENTIFICALLY ACCEPTABLE OR UNACCEPTABLE changes if the research being conducted is a clinical trial, as opposed to merely being clinical research.

### **SIGNIFICANT DIFFERENCE:**

For purposes of the NIH policies, 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.

### **SUBPOPULATIONS:**

Each minority group contains subpopulations, which 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 racial and ethnic origin. Attention to subpopulations also applies to individuals of mixed racial and/or ethnic parentage. Researchers should be cognizant of the possibility that these racial/ethnic combinations may have biomedical and/or cultural implications related to the scientific question under study.

### **VALID ANALYSIS:**

The term "valid analysis" 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.

### **WHITE:**

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