Recruitment of Special Subject Populations

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Policy/Procedure

The HS IRB recognizes the importance of its role in ensuring the equitable selection of research subjects. In fulfilling this responsibility, the HS IRB shall review the methods that investigators use to recruit Subjects and subscribe to the following guidelines:

1. RECRUITMENT OF SPECIAL SUBJECy POPULATIONS
   Federal Regulations require that the HS IRB gives special consideration to protecting the welfare of particularly vulnerable subjects, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. Investigations involving these subjects require the HS IRB and the investigator to take additional steps to assure their safety and welfare. The IRB will assign a knowledgeable reviewer to ensure the vulnerable participants are protected.

   The informed consents and assents for all vulnerable populations must still meet the requirements (45 CFR 46.116 and 21 CFR Part 50 Subpart B and Subpart D) set forth in the Informed Consent- Types and Elements SOP.

NOTE: Exempt Review
See SOP-Exempt applications for regulatory and guidance criteria for exempt research
For additional information on Exempt Review of research that involves special subject populations, please see SOP-Exempt Applications.

**Research involving Pregnant Women**

Research involving women who are or may become pregnant receives special attention from the HS IRB because of the additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. The IRB will assess the following:

a. whether the research is directed toward the mother’s health or toward the fetus; and

b. if the risks to the woman and to the fetus or neonate are minimal and when scientifically appropriate, preclinical studies including pregnant animals, and clinical studies on non-pregnant women have been conducted.

c. if the reason for excluding women is an equitable one that doesn’t deprive women from the possibility of benefiting from the study. However, women of childbearing potential may be excluded because of the concern for the welfare of the fetus, possible legal liability, and harm to mother.

d. if the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

e. if the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the Informed Consent SOP, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

No monetary incentives may be offered to induce a woman to terminate her pregnancy.

Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy

**Research involving neonates**

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

i. where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
ii. Each individual providing consent is fully informed regarding the
iii. Reasonably foreseeable impact of the research on the neonate.
iv. Individuals engaged in the research will have no part in determining
   the viability of a neonate.

Research involving Neonates of uncertain viability:

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in
research unless the following additional conditions have been met:

1. The IRB determines that (i) The research holds out the prospect of
   enhancing the probability of survival of the neonate to the point of
   viability, and any risk is the least possible for achieving that objective, or
   (ii) The purpose of the research is the development of important
   biomedical knowledge which cannot be obtained by other means and
   there will be no added risk to the neonate resulting from the research;
   and

2. Legally effective informed consent of either parent of the neonate or,
   if neither parent is able to consent because of unavailability,
   incompetence, or temporary incapacity, the legally effective informed
   consent of either parent's legally authorized representative is obtained,
   except that the consent of the father or his legally authorize
   representative need not be obtained if the pregnancy resulted from rape
   or incest.

Research involving Nonviable neonates:

After delivery nonviable neonate may not be involved in research unless all of the following
additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
ii. The research will not terminate the heartbeat or respiration of the
   neonate;
iii. There will be no added risk to the neonate resulting from the research;
iv. The purpose of the research is the development of important
   biomedical knowledge that cannot be obtained by other means; and

2. The legally effective informed consent of both parents of the
   nonviable neonate must be obtained; a legally authorized representative
   of either or both of the parents is unacceptable. A waiver and/or
   alterations of the consent do not apply. However, if either parent is
   unable to consent because of unavailability, incompetence, or temporary
   incapacity, the informed consent of one parent of a nonviable neonate
   will suffice to meet the requirements, except that the consent of the
   father need not be obtained if the pregnancy resulted from rape or incest.

Research involving, after delivery, the placenta, the dead fetus or fetal material:

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells,
tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable
federal, state, or local laws and regulations regarding such activities.
If information associated with material is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent policies are applicable.

**Research not otherwise approvable for pregnant women and fetuses, or neonates:**
The research must present an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

IRB will approve the research only if:
(a) The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and
(b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:
   1. That the research in fact satisfies the conditions of §46.204, as applicable; or
   2. The following:
      i. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
      ii. The research will be conducted in accord with sound ethical principles; and
      iii. Informed consent will be obtained in accord with the informed consent policies.

**Use of Children in Research**
The HS IRB recognizes the special vulnerability of children and takes special ethical and regulatory considerations when reviewing research projects involving this category of subjects. The IRB shall consider the benefits, risks, and discomforts inherent in the proposed research and assess their justification in light of the expected benefits to the child-subject or to society as a whole.

The IRB will determine that all regulatory criteria are satisfied for the use of children in research and documented by completing the applicable checklists. The determinations also will be documented in the minutes.

The IRB will assess the Degree of Risk in relation to the Benefit derived from participating in the research. The federal regulations require the IRB to classify research involving children into one of the four categories and to document their discussions of the risks and benefits of the research study. The four categories of research involving children based upon the degree of risk and benefit to the subjects is:

**Research Categories:**

f. **LEVEL I** Research not involving greater than minimal risk. [45 CFR 46.404 and 21 CFR 50.51] is approvable provided:
   i. Adequate provisions are made to solicit the assent of the children and permission of the parents or guardians in accordance of 21 CFR 50.55 and or 45 CFR 46.408

   g. **LEVEL II** Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject or by a monitoring
procedure that is likely to contribute to the subject's well-being. [45 CFR 46.405 and 21 CFR 50.52]. Research in this category is approvable provided:

i. the risk is justified by the anticipated benefit to the subject; and

ii. the relationship of risk to benefit is at least as favorable as any available alternative approach

iii. Adequate provisions are made to solicit the assent of the children and permission of the parents or guardians in accordance of 21 CFR 50.55 and or 45 CFR 46.408

h. LEVEL III: Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition. [45 CFR 46.406 and 21 CFR 50.53]. Research in this category is approvable provided:

i. the risk represents a minor increase over minimal risk;

ii. the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational settings; and

iii. the intervention or procedure is likely to yield generalizable knowledge about the subject’s disorder or condition that is of vital importance of the understanding or amelioration of the subject’s disorder or condition

iv. Adequate provisions are made to solicit the assent of the children and permission of the parents or guardians in accordance of 21 CFR 50.55 and or 45 CFR 46.408

b. LEVEL IV: Research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Research that is not approvable under 45 CFR 46.404, 46.405, or 46.406 may be conducted or funded by DHHS provided that the IRB and the Secretary, after consultation with a panel of experts, finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a significant problem affecting the health and welfare of children. The panel of experts must also find that the research will be conducted in accordance with sound ethical principles and adequate provisions are made for soliciting the assent of children and the permission of the parents or guardians. [45 CFR 46.407]

If the proposed research is regulated by the FDA and does not meet the requirements of 21 CFR 50.51, 50.52 or 50.53 the research may proceed only if:

(a) The IRB finds and documents that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

(b) The Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine,
education, ethics, law) and following opportunity for public review and comment, determines either:

(1) That the clinical investigation in fact satisfies the conditions of 50.51, 50.52, or 50.53, as applicable, or

(2) That the following conditions are met:

   (i) The clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

   (ii) The clinical investigation will be conducted in accordance with sound ethical principles; and

   (iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in 50.55.

Consent and Assent Procedures

When children are involved in research, the investigator must ensure adequate provisions are made for soliciting assent of the children and permission of their parents or guardians. [45 CFR §46.408 or 21 CFR §50.55]. (For requirements of informed consent see Informed Consent – Types and Elements SOP and Informed Consent – Process and Issues SOP) The IRB must:

a. In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research.

a. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

b. A written assent document should include:

   a. an explanation of the proposed research procedures in a language specific, understandable, and appropriate for the age, experience, maturity, and condition of the child.

   b. an explanation of the benefits of the research.

   c. an explanation of the risks, discomforts, and inconveniences associated with the research;
Assent Waiver
Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.
For studies regulated by the FDA, under 21 CFR 50.55 the assent may be waived if it finds and documents that:
1) The clinical investigation involves no more than minimal risk to the subjects;
2) The waiver will not adversely affect the rights and welfare of the subjects;
3) The clinical investigation could not practicably be carried out without the waiver; and
4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Parental Permission
b. The IRB shall determine, in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405. Where research is covered by §46.406 and §46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. Permission by parents or guardians must be documented in accordance with and to the extent required by 46.117 of Subpart A.

For studies regulated by the FDA:
1) Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient, if consistent with State law, for clinical investigations to be conducted under 50.51 or 50.52.
2) Where clinical investigations are covered by 50.53 or 50.54 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child if consistent with State law.
3) Permission by parents or guardians must be documented in accordance with and to the extent required by 50.27.

In addition to the provisions for waiver contained in §46.116 of subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the
protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

Note: Parental or guardian permission cannot be waived in FDA regulated studies and consent must be documented in accordance with and to the extent required by 50.27.

Research involving Wards of the State

Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if such research is:

(1) Related to their status as wards; or
(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(b) If the research is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

For studies regulated by the FDA:

(a) Children who are wards of the State or any other agency, institution, or entity can be included in clinical investigations approved under 50.53 or 50.54 only if such clinical investigations are:

(1) Related to their status as wards; or
(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(b) If the clinical investigation is approved under paragraph (a) of this section, the IRB must require appointment of an advocate for each child who is a ward.

(1) The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis.
(2) One individual may serve as advocate for more than one child.
(3) The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the clinical investigation.
(4) The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the clinical investigation, the investigator(s), or the guardian organization.
Use of Prisoners in Research

The HS IRB recognizes that research involving prisoners raises the issue of whether the subjects situation prohibits the exercise of free choice to participate in research and whether or not the prisoners confidentiality will be adequately maintained. The IRB has appointed a prison representative with the appropriate background, who is a voting member of the board, to review the proposal and consult on behalf of the prisoner’s rights. The majority of the members of the IRB will have no association with the prison involved in the research except in the context of being a member of the IRB.

When reviewing research with the use of prisoners, minimal risk is defined as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

When reviewing research involving prisoners, the IRB shall:

a. Have IRB staff assure that the person designated as the prisoner representative, with the appropriate background to review the proposal, reviews protocols involving prisoners, is present during the board meeting, using utilizing the appropriate prisoner forms for prisoner research and consult on behalf of the prisoner’s rights;

b. Ensure that the research MUST fit into one of the four categories:
   a. Category I: Studies of the possible cause, effects, and processes of incarceration and criminal behavior, and involves no more than minimal risk with no more than inconvenience to the subjects;
   b. Category II: Studies of prisons as institutional structures or of prisoners as incarcerated persons, and involves no more than minimal risk no more than inconvenience to the subjects;
   c. Category III: Studies on particular conditions affecting prisoners as a class; (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; or
   d. Category IV: Studies involving a therapy likely to benefit the prisoner subject Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of the intent to approve such research.
(c) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

(d) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

(e) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

(f) The information is presented in language which is understandable to the subject population;

(g) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

(h) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

(i.) The Board shall carry out such other duties as may be assigned by the Secretary.

(ii.) The institution shall certify to the Secretary, in such form and manner as the Secretary may require, that the duties of the Board under this section have been fulfilled.

Use of Cognitively Impaired Persons:

The HS IRB appreciates the ethical concerns in research involving individuals that are cognitively impaired which may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participating in research. When reviewing the study, the board will determine:

a. if the subject population is appropriate for the study
b. require the investigator to specifically describe the psychological or medical screening criteria
c. Assure that the investigator satisfies the Informed Consent criteria:
   a. Presume the subject is competent to consent unless there is evidence of serious mental disability that would impair reasoning or judgment.
      i. Obtain consent from the legally authorized individual (see Informed Consent –Process and Issues SOP regarding Legally Authorized Representatives)
d. Seek a legal consultant to determine the applicable laws of the state, if needed.
e. Seek the subject’s assent where applicable
f. The IRB will assess the proposed plan for the determination of whether the participant has the capability to consent or assent and determine if the plan for assent is adequate.
g. if the subjects are institutionalized, the study must be reviewed full board
h. determine if any additional safeguards are necessary

Use of Students and Employees

The HS IRB recognizes the special concerns that may present when students participate in research projects. Since the federal regulations do not provide explicit protections for these subjects, the IRB shall take extra measures to ensure the safety and welfare for students. The IRB will:
   a. Pay special attention to protect against coercion and offense to the voluntary requirement for research involving humans:
   b. Add heightened scrutiny for projects requiring participation in the research project for course credit to assure the participants are not coerced to participate;
   c. In research projects that offer extra-credit for participation, the investigator must provide an comparable alternate method of credit for a student declining to participate:
      a. The paper may not be graded and receive the same amount of points as research participants do, however, the quality and quantity of time devoted to the paper should be worthy in comparison to the study participant’s investment of time;
      b. The student shall not lose the extra credit if they withdraw from the study;
   d. The investigator should consider recruiting subjects through general announcements or advertisements, rather than through individual solicitations or classroom solicitations.
   e. The study must be minimal risk

Employees Involved in Research

The issues with respect to employees as research subjects are essentially identical to those involving students as research subjects, in that employee research programs may raise the possibility that the decision will affect performance evaluations or job advancement. It may also be difficult to maintain the confidentiality of personal medical information or research data when the subjects are also employees.

Use of Low-Income Persons

The HS IRB realizes the importance of achieving an equitable representation of subjects involved in research, and may create special concerns during the review process. The IRB will assure that:
   a. Avoidance of coercion and undue influence upon subjects to participate;
   b. Assess the mechanism for offering incentives of value to the subjects:
   c. The subject’s privacy rights and confidentiality are addressed.
d. Opportunity for reasonable alternatives are available.

Use of Minorities

The HS IRB is aware that members of racial and ethnic minority groups raise concerns about appropriate levels of inclusion and generalizability of study results, similar to the inclusion of women in studies. The involvement of minorities in research may raise concerns about the selection of subjects, the possibility of special vulnerability on the part of some prospective subjects, and about consent and the relative strengths and weaknesses of vulnerable groups in the consent process.

Investigators must provide:

a. A clear compelling rationale for their exclusion or under representation of the subject.
b. Select an equitable choice of a geographic area for recruitment must be representative of the racial and ethnic groups in study populations;
c. Safeguard the consent process to ensure open and free communication:
   a. Written in a language specific to the population
d. Consider cultural norms when instituting the consent policy.

Use of Elderly/Aged Persons

The HS IRB realizes that the participation of the Elderly and Aged subjects in research poses several issues for consideration, primarily whether the subject needs special protections. The IRB must balance the need to protect with the need to provide respect for persons. There is no age requirement at which time prospective subjects should become ineligible to participate in research, therefore the inclusion of elderly subjects in research is very important. The IRB shall:

a. Take special consideration to closely monitor research conducted in nursing homes or other institutions, unless the involvement of the institutional population is necessary to the conduct of the research.
b. The IRB may consult with an expert on this subject prior to making a determination about the research.

a. International Research

All human subjects’ research in which American investigators are involved, and which would be subject to the federal regulations if it were conducted wholly within the United States, must comply with the federal regulations for the protection of human subjects in all material respects.