

Title:	Review of Human-Subjects Research Involving Vulnerable Populations
Department:	Human Research Affairs
Policy Type:	<input checked="" type="checkbox"/> Partners System-wide <input type="checkbox"/> Partners System-wide Template <input type="checkbox"/> Partners HealthCare <input type="checkbox"/> Partners HealthCare Departmental <input type="checkbox"/> Institution
Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Faulkner Hospital (FH), Massachusetts General Hospital (MGH), McLean Hospital (McLean), and North Shore Medical Center (NSMC)
Approved by:	Chief Academic Officer
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Contact Person:	Director, Human Research Review and Compliance

KEYWORDS:

IRB, Institutional Review Board

PURPOSE:

The purpose of this policy is to define the procedures the Partners Human Research Committees (PHRC) follow when reviewing human-subjects research and clinical investigations involving pregnant women or human fetuses, nonviable neonates and neonates of uncertain viability, prisoners, and children.

DEFINITIONS:

See Definition of Human-Subjects Research

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102(i)][21 CFR 56102(i)]

POLICY STATEMENT:

The PHRC will approve human-subjects research and clinical investigations that involve the inclusion of pregnant women or human fetuses, nonviable neonates or neonates of uncertain viability, prisoners, or children only if the PHRC finds and documents that the research satisfies the conditions of 45 CFR 46, Subpart B, C, and D and, when applicable, 21 CFR 50 Subpart D, and applicable State law.

PROCEDURES:

Investigators relying on the PHRC for IRB review of human-subjects research and clinical investigations are required to provide the PHRC with all applicable forms and documents required for review of research involving vulnerable populations.

Pregnant Women or Fetuses

Pregnant women or fetuses may be involved in research if all of the regulatory conditions are met, as quoted below:

1. Federal Regulations 45 CFR 46.204
 - (a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
 - (b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or if there is no such prospect of direct benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
 - (c) Any risk is the least possible for achieving the objectives of the research;
 - (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, her consent is obtained in accord with the informed consent provisions of subpart A;
 - (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 provisions of subpart A of this part, 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.
 - (f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
 - (g) For children as defined in 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;
 - (h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
 - (i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
 - (j) Individuals engaged in the research will have no part in determining the viability of a neonate.

2. **State Law M.G.L. ch. 112, s. 12J(a)**

Research involving human fetuses is also subject to state law M.G.L. 112C:12J(a), as quoted in relevant part below:

- I. No person shall use any live human fetus whether before or after expulsion from its mother's womb, for scientific, laboratory, research or other experimentation. This section shall not prohibit procedures incident to the study of a human fetus while it is in its mother's womb or a neonate;

provided that in the best medical judgment of the physician, made at the time of the study, the procedures do not substantially jeopardize the life or health of the fetus or neonate, and provided further that, in the case of a fetus, the fetus is not the subject of a planned abortion.

This section shall not prohibit or regulate diagnostic or remedial procedures the purpose of which is: (i) to determine the life or health of the fetus or neonate involved; (ii) to preserve the life or health of the fetus or neonate involved or the mother involved; (iii) to improve the chances of a viable birth for a fetus with a congenital or other fetal conditions that would otherwise substantially impair or jeopardize the fetus's health or viability; or (iv) research approved by an institutional review board applying federal regulations for the protection of fetuses and neonates, that are conducted for the purpose of developing, comparing or improving diagnostic or therapeutic fetal or neonatal interventions to improve the viability or quality of life of fetuses, neonates and children.

- II. No experimentation shall knowingly be performed upon a dead fetus or dead neonate unless the consent of the parent or guardian has first been obtained, provided, however, that such consent shall not be required for a routine pathological study.
- III. No person shall perform or offer to perform an abortion where part or all of the consideration for said performance is that the fetal remains may be used for experimentation or other kind of research or study.
- IV. No person shall knowingly sell, transfer, distribute or give away any fetus or neonate for a use which is in violation of this section.

Neonates

Neonates may be involved in research if all of the federal and state requirements are met as described below.

1. Federal Regulations 45 CFR 46.205
 - (a) Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:
 - (1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
 - (2) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and
 - (3) Individuals engaged in the research will have no part in determining the viability of a neonate.
 - (b) Neonates of uncertain viability may not be involved in research unless:
 - (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) The 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 consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
 - (c) Nonviable neonates may not be involved in research unless all of the following additional conditions are met:
 - (1) Vital functions of the neonates will not be artificially maintained;

- (2) The research will not terminate the heartbeat or respiration of the neonate;
 - (3) There will be no added risk to the neonate resulting from the research;
 - (4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
 - (5) The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46 subpart A, except that the waiver and alteration provisions of 46.116(c) and (d) 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. Consent of the father need not be obtained if the pregnancy resulted from rape or incest. Consent cannot be obtained from a legally authorized representative.
- (d) Viable neonates may be included in research only to the extent permitted by 45 CFR 46 Subpart D - Additional Protections for Children Involved as Subjects in Research.

2. State Law M.G.L. ch. 112, s. 12J

The PHRC will also consider research involving neonates under M.G.L. ch. 112, s. 12J, as quoted in relevant part above.

Pregnant Women or Fetuses and Neonates

Federal Regulations 45 CFR 46.207 Pregnant women, fetuses or neonates

Pregnant women, fetuses, or neonates may be involved in research not otherwise approvable under 45 CFR 46.204 or 45 CFR 46.205 only if the IRB finds that the research presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates and, if HHS-funded, the research is submitted to the Secretary of HHS for consultation with a panel of experts in pertinent disciplines and opportunity for public review and comment. When the research is funded by a federal agency other than HHS, the IRB will consult with appropriate officials at the relevant federal agency or department funding the research.

When the research is supported by a non-federal sponsor, the IRB will consider convening a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and provide an opportunity for review and comment by the local community where the research is to be conducted before deciding whether to proceed with the research,

Prisoners

Research involving prisoners can only be approved by an IRB that satisfies the following regulatory requirements in 45 CFR 46.304, as quoted in part below:

- (a) The majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.
- (b) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

“Prisoner” is defined by HHS regulations at 45 CFR 46.303(c) as “any individual involuntarily confined or detained in a penal institution”. Guidance provided by OHRP extends the definition to individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

The PHRC will rely on the IRB of the Harvard School of Public Health (HSPH) for review of research involving prisoners until such time as the PHRC includes a prisoner representative. The HSPH review

conforms to the requirements of 45 CFR 46, including the additional protections for prisoners outlined in subpart C.

If during the course of the research, an individual subject becomes a “prisoner” as defined above, the investigator is required to notify the PHRC promptly. At that point the investigator must discontinue all research activities with the subject unless the investigator asserts in writing and the reviewing PHRC Chairperson agrees in writing that it is in the best interests of the subject to continue to participate in the research while the research is being re-reviewed by the HSPH IRB in accordance with the additional protections for research involving prisoners.

In making this determination the reviewing PHRC Chairperson will consider (1) whether the research involves an intervention or procedure that holds out a prospect of direct benefit that is important to the health or well-being of the individual and is available only in the context of the research and (2) whether the research can be performed safely while the individual is a prisoner.

Children

Consistent with Massachusetts State Law that allows persons who have attained the age of 18 to consent to treatment or procedures, the PHRC defines children as persons under the age of 18. The PHRC notes, however, that certain statutes and case law provide children with majority status for medical decision-making in some circumstances, for example: emancipated minor; mature minor; or minor seeking care for drug addiction, sexually transmitted diseases, emotional disorders, or abortion. Because Massachusetts law and the applicable Partners-affiliated entities’ policies do not specifically address consent of children with majority status to research, the PHRC will review issues of consent related to the enrollment of children with majority status on a case-by-case basis.

The PHRC may approve research that involves children as subjects of research if regulatory requirements at 45 CFR 46 Subpart D and 21 CFR 50 Subpart D are met, as quoted in part below:

1. 46.404 / 50.51: Research not involving greater than minimal risk;
2. 46.405 / 50.52: Research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects; or
3. 46.406 / 50.53: Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition.
4. 46.407 / 50.54: Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. HHS-funded research in this category must be submitted to the Secretary of HHS and/or Commissioner of Food and Drugs for consultation with a panel of experts in pertinent disciplines and opportunity for public review and comment. When the research is funded by a federal agency other than HHS, the IRB will consult with appropriate officials at the relevant federal agency or department funding the research.

When the research is supported by a non-federal sponsor, the IRB will consider convening a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and provide an opportunity for review and comment by the local community where the research is to be conducted before deciding whether to proceed with the research.

The PHRC must determine whether permission of one or both parents must be obtained for participation of the children in the research. When the research is covered by 46.404 / 50.51 or 46.405 / 50.52, the PHRC may determine that permission of one parent is sufficient. When the research is covered by 46.406 / 50.53 or 46.407 / 50.54, permission of both parents must be obtained 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.

The PHRC must also determine whether assent of the children participating in the research is required. When making determinations regarding assent, the PHRC will consider the capacity of the children to assent, taking into consideration the age, maturity and psychological state of the children involved. Determinations regarding assent may be made for all of the children participating in the research or for each child. When the PHRC determines that assent is required, the PHRC determines whether assent will be documented and if so, the process to document assent. When the research holds out the 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 necessary for proceeding with the research.

Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 46.407 and 21 CFR 50.53 or 50.54 only if the 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.

If the research is approved based on the paragraph above regarding children who are wards, the PHRC will 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 will 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 research and who is not associated in any way (except in the role as advocate or member of the PHRC) with the research, the investigator(s), or the guardian organization. In Massachusetts, parents of children in Department of Children and Families (DCF) care or custody generally retain the right to consent to participation by their child in any medical or psychological research; DCF / DCF staff cannot provide consent. When DCF has custody pursuant to surrender or termination of parental rights, or when parents cannot be located, DCF must seek judicial approval in order for the child to be enrolled.

OTHER APPLICABLE PARTNERS HEALTHCARE POLICIES:

Informed Consent of Research Subjects

REFERENCE:

45 CFR 46, Subparts B, C, D
 21 CFR 50, Subpart D

DEVELOPMENT AND CONSULTATION

Human Research Office
 Office of the General Counsel

Reviewed by:	Original Review Date:	Revision Approval Dates:
Dennis A. Ausiello, MD, Chief Scientific Officer	December 16, 2010	
Anne Klibanski, MD, Chief Academic Officer		May 5, 2015