

PARTNERS HUMAN RESEARCH COMMITTEE POLICIES AND PROCEDURES

Research Involving Vulnerable Populations

1.0 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 vulnerability, prisoners, and children.

2.0 SCOPE

Non-exempt human-subjects research and clinical investigations reviewed by the PHRC are subject to this policy.

3.0 DEFINITIONS

As used in this document, human-subjects research encompasses activities that meet the DHHS definitions of *research* and *human subject* and/or the FDA definitions of *clinical investigation* and *human subject*. The DHHS definition for *research* and *human subject* and the FDA definition for *clinical investigation* and *human subject* are provided below.

Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(d)]

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. [45 CFR 46.102(f)(1)(2)]

Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous... [21 CFR 50.3(c) and 21 CFR 56.102(c)]

Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

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 56.102(i)]

4.0 POLICY

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 21 CFR 50 Subpart D, when applicable, and applicable State law.

5.0 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.

5.1 Pregnant Women or Fetuses

Pregnant women or fetuses may be involved in research if all of the regulatory conditions in 45 CFR 46.204 are met, as quoted below:

- (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.

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

Experimentation on human fetuses is also subject to state law M.G.L. 112C:12J(a), as quoted in 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 kind of experimentation. This section shall not prohibit procedures incident to the study of a human fetus while it is in its mother's womb provided that in the best medical judgment of the physician, made at the time of the study, said procedures do not substantially jeopardize the life or health of the fetus, and provided said 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 to determine the life or health of the fetus involved or to preserve the life or health of the fetus involved or the mother involved.

- II. No experimentation may knowingly be performed upon a dead fetus unless the consent of the mother has first been obtained, provided, however, that such consent shall not be required in the case of 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 [as defined in M.G.L. ch. 112, s. 12J] for a use which is in violation of the provisions of this section.

5.2 Neonates

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

5.2.1 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 CRF 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.

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

The PHRC will consider the application of M.G.L. ch. 112, s. 12J to the research, consulting with the Partners Office of General Counsel as necessary.

5.3 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 Chairpersons agree 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 Chairpersons 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.

5.4 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 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 BWH/MGH 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 46.404, 405, 406 and 21 CFR 50.51, 52, 53 are met, as quoted in part below:

- Research not involving greater than minimal risk;
- Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects; or
- 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.

The PHRC may submit research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children 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 as outlined in 45 CFR 46.407 and 21 CFR 50.54.