
Yale University Institutional Review Boards

IRB Policy 330 Inclusion of Pregnant Women, Women of Childbearing Potential, Fetuses and Neonates in Research

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Policy Sections	2
330.1 Requirements for Approval of DHHS-funded Biomedical or Behavioral Research Involving Pregnant Women or Fetuses	2
330.2 IRB Requirements for non-DHHS-funded, or non-Biomedical or Behavioral Research Involving Pregnant Women.....	3
330.3 IRB Findings for Approval of Research Involving Neonates.....	3
330.4 IRB Approval of Research Involving, after Delivery, the Placenta, the Dead Fetus or Fetal Material	4
330.5 Research Not Otherwise Approvable	5
Special Situations/Exceptions	6
Pregnant Children	6
Women of Childbearing Potential: Reproductive Risks.....	6
Studies to Develop or Evaluate Methods of Enhancing Conception or Contraception	6
In Vitro Fertilization.....	6

Scope

This policy defines the additional protections required for the participation of pregnant women, fetuses, and/or neonates, as well as women of childbearing potential, in biomedical, behavioral, and social science research. The policy is applicable for all human research intending to study pregnant women, fetuses and/or neonates, or involving women of childbearing potential.

Policy Statement

Research that permits the enrollment of women who are or may become pregnant or that is directed toward a fetus or neonate requires special attention when it is necessary to protect the rights and welfare of the pregnant women and/or the fetus and/or neonate. The IRB will approve Department of Health and Human Services (DHHS) funded research which focuses on pregnant women or fetuses if, in addition to meeting all other requirements, the research satisfies the conditions of 45 CFR 46, Subpart B, which are described below. The IRB will approve research involving pregnant women, fetuses and/or neonates that is not funded by DHHS after applying criteria described herein and determining that the criteria herein are satisfied or approval for alteration of or variation from these criteria is justified. The IRB will approve research involving women who may become pregnant if appropriate safeguards are in place to protect against the risk of pregnancy, should pregnancy be a specific exclusionary criterion.

Reason for the Policy

Pregnant women, fetuses and neonates are considered vulnerable populations. Research that incorporates any conditions for the inclusion of pregnant women or women who may become pregnant requires special attention from the investigator and IRB because of the additional health concerns women face during pregnancy and the need to avoid unnecessary risk to the fetus. Special attention is also required because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society. Additional safeguards beyond the basic requirements for protecting human participants are prescribed in the federal regulations for research involving pregnant women at [45 CFR 46 Subpart B](#), enforced by the Office for Human Research Protections (OHRP). These regulations also cover research using human fetal tissue, placenta or post-delivery fetal material. For research not funded by DHHS, no additional safeguards are required and there are no restrictions on the involvement of pregnant women in research where the risk to the fetus is no more than minimal. However, additional safeguards as described by the federal regulations will be applied, as appropriate, on a case-by-case basis by the IRB when reviewing studies involving greater than minimal risk to the fetus.

Definitions

Pregnancy

For purposes of this policy, the period of time from implantation until delivery.

Fetus

The product of conception from the time of implantation until delivery.

Legally Authorized Representative

An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Surrogate Consent

Consent for an individual to participate in research given by an appropriate surrogate (e.g., next of kin – spouse, parent, child, sibling) when an individual is assessed as not capable of providing fully informed and legally effective consent.

Neonate

A newborn.

Nonviable neonate

A neonate after delivery that, although living, is not viable.

Viable

Pertaining to neonates and for purposes of this policy, the ability, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. If a neonate is viable, it may be included in research only to the extent permitted and in accordance with the requirements of Subparts A (Basic DHHS Policy for Protection of Human Research Subjects) and D (Additional Protections for Children Involved as Subjects in Research) of 45 CFR 46.

Policy Sections

330.1 Requirements for Approval of DHHS-funded Biomedical or Behavioral Research Involving Pregnant Women or Fetuses

Research involving pregnant women or women of childbearing potential may be approved by the IRB once the following determinations are made and the findings are documented:

1. 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 the risk/benefit assessment for pregnant women and fetuses;
2. When the research has the potential of directly benefiting the woman or the fetus, a greater than minimal risk to the fetus is acceptable. If the research does not hold the prospect of directly benefiting the woman or fetus, then the research is allowed if 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;
3. Any risk is the least possible for achieving the objectives of the research;
4. The pregnant woman's consent is sufficient when there is the prospect of direct benefit for the pregnant woman, the pregnant woman and the fetus, or when there is no prospect of benefit for the woman or the fetus but the 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,
5. When the research has the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father of the fetus is required in accordance with the informed consent provisions of IRB Policy 200, except that the father's consent is not required if he is unable to

consent because of unavailability, incompetence, or temporary incapacity, or the pregnancy resulted from rape or incest;

6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. In the case of pregnant females who are themselves minors (under age 18), assent and permission are obtained in accordance with IRB Policy 310: Participation of Children in Research;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. 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
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

DHHS-funded biomedical or behavioral research that does not meet the above qualifications may only be conducted with approval of the Secretary of U.S. Department of Health and Human Services (see Section 330.5 below).

330.2 IRB Requirements for non-DHHS-funded, or non-Biomedical or Behavioral Research Involving Pregnant Women

The IRB recognizes that some types of research that could be conducted with pregnant women do not fit squarely within the regulatory requirements for approval. For example, minimal risk research involving interviews, surveys, oral histories and other social, behavioral, and educational research, as well as research that does not intend to develop important biomedical knowledge, is not addressed in the regulations under Subpart B. The IRB also recognizes that some research that targets a wide population may coincidentally encounter pregnant women as potential research participants, yet does not present additional risks to participants who are or may become pregnant. Additionally, the IRB acknowledges that some types of biomedical research that present minimal or greater than minimal risk to pregnant women or fetuses do not meet all ten criteria for approval under Subpart B. When these types of extra-regulatory circumstances apply, the IRB can consider approving the research if DHHS does not fund the studies, since the review criteria set forth under Subpart B are not applicable and the IRB does not require the criteria to be met for approval. However, investigators and the IRB will nonetheless consider the research in light of the inclusion of pregnant women, and the IRB will use the criteria as a framework in determining approval. The IRB may waive some or all of the Subpart B requirements for non-DHHS funded research on a case-by-case basis or even for certain classes of research as deemed appropriate to the risks.

330.3 IRB Findings for Approval of Research Involving Neonates

Research involving newborns (neonates) of uncertain viability and nonviable newborns may be approved by the IRB once the following determinations are made and the findings are documented:

- (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 under Section 1 or 2 below is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- (3) Individuals engaged in the research will have no part in determining the viability of a neonate.
- (4) The requirements of Sections 1 and 2 below have been met, as applicable.

1. 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) 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 IRB may approve the substitution of the informed consent of either parent's surrogate or legally authorized representative being obtained; except that the consent of the father or his surrogate or legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

2. Nonviable neonates

After delivery the 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;
- (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 Policy 200: Informed Consent for Human Research, except that the waiver and alteration provisions 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, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will **not** suffice to meet these requirements.

3. Viable neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of Policy 200: Informed Consent for Human Research, and Policy 310: Participation of Children in Research.

330.4 IRB Approval of Research Involving, after Delivery, the Placenta, the Dead Fetus or Fetal Material

The IRB is required to review and approve research involving the placenta, dead fetus or macerated fetal material, or cells, tissue, or organs excised from a dead fetus if information associated with this material is recorded for research purposes in a manner that living individuals (e.g., parents, siblings) can be identified, directly or through identifiers linked to those individuals. If such identification is possible, then those individuals are research subjects and all pertinent federal regulations involving human research subjects are applicable. (45 CFR 46.206). The research shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

Federal Laws Governing Research on Transplantation of Fetal Tissue

Federal law which may apply to research involving fetal tissue requires that, for research carried out on human fetal tissue, the woman providing the tissue makes a signed statement declaring that:

- the woman donates the fetal tissue for use in research;
- the donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue; and
- the woman has not been informed of the identity of any such individuals.

Furthermore, the tissue may be used only if the individual with the principal responsibility for conducting the research (the principal investigator) makes a signed statement declaring that he/she:

(1) is aware that:

- the tissue is human fetal tissue;
- the tissue may have been obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth; and
- the tissue was donated for research purposes.

(2) has provided such information to other individuals with responsibilities regarding the research;

(3) will require, prior to obtaining the consent of an individual to be a recipient of a transplantation of the tissue, written acknowledgment of receipt of such information by such recipient; and

(4) has had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy made solely for the purposes of the research.

Investigators contemplating research involving human fetal tissue should consult PUBLIC LAW 103-43; JUNE 10, 1993: RESEARCH ON TRANSPLANTATION OF FETAL TISSUE, SEC. 498A (<http://www.hhs.gov/ohrp/humansubjects/guidance/publiclaw103-43.htm>).

Embryonic Stem Cell Research

Research involving human embryonic stem cells must be approved by the Yale human Embryonic Stem Cell Research Oversight Committee (ESCRO) and comply with all requirements prior to its undertaking. Investigators should consult the University's Policy for Review of Human Embryonic Stem Cell Research at Yale, which applies to the conduct of human embryonic stem cell (hESC) research and to all persons who conduct hESC research as Yale students, faculty or staff, using Yale facilities, or paid for with Yale funds. See <http://www.yale.edu/provost/html/escropolicy.html>.

330.5 Research Not Otherwise Approvable

Research that is funded by DHHS and does not meet the aforementioned approval criteria must be approved by the Secretary of Health and Human Services (45 CFR 46.207). If 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 the research is not approvable under the above provisions, then the research will be sent to OHRP for the review and approval by the Secretary of Health and Human Services.

Special Situations/Exceptions

Pregnant Children

In Connecticut, pregnant females who are minors (under age 18) may consent to treatment concerning their pregnancy without parental knowledge or permission. The IRB will consider on a case-by-case basis the appropriateness of involving pregnant minor females in research, and approve such research only after careful deliberation with pediatric and obstetric specialists on the board. In other jurisdictions, investigators should consult local law.

Women of Childbearing Potential: Reproductive Risks

National Institutes of Health (NIH) policy requires the inclusion of women in research study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study [PHS Grant Application form 398, pp. 21-22]. Where research involves potential risk sufficient to justify requiring that pregnant women either be specifically excluded or studied separately, prospective study participants should be tested for pregnancy and warned about possible and/or unknown reproductive or lactation risks from study treatments. Investigators must discuss these risks and the steps taken to minimize them in both the consent form and in the protocol application. Subjects should be advised to notify the investigator immediately should they become pregnant. (See Guidance: 330 GD. 1 Reproductive Risks and Contraception for more information.)

Studies to Develop or Evaluate Methods of Enhancing Conception or Contraception

These studies are closely related to research involving pregnant women and raise some of the same concerns. There are no special regulations for this category of research, but special IRB attention is needed. IRBs should ensure that there is an adequate explanation of the risks, benefits, reversibility, and alternatives; that backup protection against unintended pregnancy is provided when appropriate; and that the possibility of failure (and options available for dealing with unintended pregnancies) are satisfactorily described.

In Vitro Fertilization

While in vitro fertilization (IVF) research is not currently supported by federal funding or protected by federal law, some Yale investigators may be involved in privately-funded research on IVF as a treatment for infertility or other problems. In such cases, investigators are still required to seek IRB review and approval before initiating such human research. A critical consideration in IVF research is assuring that, where gamete donors are known, an agreement exists between donors and recipients. Additionally, investigators should be aware that embryos that are being studied at temperatures that allow them to develop cannot be studied beyond 14 days old. The American Society for Reproductive Medicine (<http://www.asrm.org/>) is a recommended resource for investigators to consult for ethical guidance for IVF research.

Related Information

IRB Policy 200: Informed Consent for Research Involving Human Participants

IRB Policy 310: Participation of Children in Research

Policy for the Review of Human Embryonic Stem Cell Research at Yale

330 CH 1: Worksheet for Studies Involving Pregnant Women, Fetuses and Neonates in Research

330 PR 1: Inclusion of Pregnant Women or Women of Childbearing Potential in Research

330 GD 2: Guidance on Reproductive Risk and Contraception for Women Involved in Research

http://www.hhs.gov/ohrp/irb/irb_chapter6.htm

Contacts

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IRB Review of Social Science, Behavioral, Education and Humanities Research	Human Subjects Committee	203-436-3650 Human.subjects@yale.edu

Roles and Responsibilities

[Human Investigation Committee:](#)

The HIC I, HIC II, HIC III and HIC IV serve as the four Institutional Review Boards or IRBs for biomedical human research conducted at Yale University.

[Human Subjects Committee:](#)

The HSC is responsible for the review and oversight of social and behavioral research involving human participants.

Revision History