

Wayne State University Human Investigation Committee	
Subject	The Inclusion of Pregnant Women in Research
Form Date	Revised 7/21/10
Approvals	10/21/97 Steering Committee, 12/4/97 All IRB Committees, 4/25/98 Administrative Approval, 9/30/10 Administrative Approval

Background

In accordance with its dedication to the highest levels of research integrity, all research at Wayne State University is conducted in compliance with the principles of the Belmont Report and other ethical codes of conduct for research, such as the Declaration of Helsinki and the Nuremberg Code, and is consistent with Good Clinical Practice (GCP) guidelines. Wayne State has made a commitment to conduct *all* research, regardless of sponsorship, under these principles and all relevant local, state, federal and international regulations in order to provide the same high level of protection for all human participants.

Based on federal regulations described in Title VII of the Civil Rights Act of 1964 and Pregnancy Discrimination Act of 1978, it is illegal to discriminate against individuals on the basis of sex and/or pregnancy. By implication and logical extension, the *automatic* exclusion of pregnant women from research protocols is discriminatory and therefore illegal.

Sections of the Code of Federal Regulations [45 CFR 46.206(a)(2) and 45 CFR 46.207] also address some issues concerning the inclusion of pregnant women in clinical research. These regulations are clear when the protocol offers the possibility of saving a woman's life, but they are more general in other circumstances. The Code also states that the decision to participate is the woman's, but the father's consent should be obtained in some circumstances. It stipulates the circumstances under which a father's consent is not necessary. See HIC Policy/Procedure: "Research Involving Fetuses and Neonates" for related HIC policy.

HIC Policy

A pregnant woman cannot be excluded from a protocol if saving her life is even a remote possibility, and *there are not other equivalent therapeutic alternatives*.

A pregnant woman may be excluded from a research protocol *IF* appropriate studies on animals and non-pregnant individuals have not been completed. Exceptions to this stipulation are as follows:

1. The purpose of the activity is to meet the health needs of the mother and the fetus will be placed at risk only the minimum extent necessary to meet such needs;

OR

2. The risk to the fetus is minimal.

When considering the health needs of the mother, the risk-benefit ratio of the research activity for the individual and the fetus must be considered in the context of available alternatives.

Environmental Protection Agency (EPA) requirements:

- EPA prohibits research involving the intentional exposure of pregnant women, nursing women, or children to any substance.
- EPA requires application of 40 CFR 26 Subparts C and D to provide additional protections to pregnant women and children as participants in observational research (i.e., research that does not involve intentional exposure to any substance).
- EPA policy requires submission of IRB determinations and approval to the EPA Human Subjects Research Review official for final review and approval before the research can begin.
- For research not conducted or supported by any federal agency that has regulations for protecting human research participants and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research participants apply, including:
 - EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance.
 - EPA prohibits the intentional exposure of pregnant women, nursing women, or children to any substance.

Department of Defense (DoD) funded research requirements:

The DoD applies the provisions in 45 CFR 46, Subparts B, C, and D for the protection of vulnerable classes of subjects. For further information, please see the DoD Directive 3216.02 when human research is conducted or supported by a DoD component (an organizational entity within the DoD).

HIC Policy for IRB Review of Protocols

Each protocol must be reviewed individually to determine whether the decision to include or exclude pregnant women in that particular study is appropriate in the context of available alternatives. The automatic exclusion of pregnant women (i.e., without a stated rationale) is not acceptable. Reviewers should ask the investigator for an explanation of the rationale for inclusion or exclusion if it is not given or if it is not clear. The rationale must be scientifically justifiable. The following guidelines are to be followed in considering the inclusion of pregnant women in individual protocols:

- If the protocol offers the chance of saving a woman's life, and there are not equivalent available therapeutic alternatives, she cannot be excluded from the study on the basis of her pregnancy.
- If the protocol offers the chance of meeting the health needs of a woman **AND** the fetus will be placed at risk only to the minimum extent necessary to meet such needs, she cannot be excluded on the basis of pregnancy.
- If the protocol would result in only minimal risk to the fetus, a woman cannot be automatically excluded on the basis of her pregnancy.

Environmental Protection Agency (EPA) Sponsored Research

- For research conducted or supported by the EPA, research involving intentional exposure of pregnant women or children to any substance is prohibited and not approved by the IRB.
- For research intended for submission to the EPA, research involving intentional exposure of pregnant women or children to any substance is prohibited and not approved by the IRB.
- The IRB reviews observational research involving pregnant women and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B.
- The IRBs may review and approve observational research involving children that does not involve greater than minimal risk only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 40 CFR 26.406.
- The IRB may review and approve observational research involving children that involves greater than minimal risk but presenting the prospect of direct benefit to the individual participants if the IRB finds that:
 - The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to the participant's well-being.
 - The risk is justified by the anticipated benefit to the participants.
 - The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
 - Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 40 CFR 26.406.

HIC Policy on Informed Consent:

Once it has been determined that pregnant women may be included in a protocol, the decision to participate is the mother's (45 CFR 46.207). However, the father's consent should also be obtained **EXCEPT** under any of the following circumstances:

1. The purpose of the research is to meet the health needs of the mother and his refusal would interfere with this.
2. The father's identity or whereabouts cannot reasonably be ascertained.
3. He is not reasonably available.
4. The pregnancy resulted from rape.
5. The risk to the fetus is minimal.

The mother and father must be legally competent. If the father's consent is required, his signature should be added to the consent form; if not, the basis for the exception should be noted on the form.

Per ICH-GCP (E6) guidance, the following applies:

- When adults are unable to consent, the IRB must determine:
 - A non-therapeutic clinical trial (i.e., a trial in which there is no anticipated direct clinical benefit to the participant) should be conducted in participants who personally give consent and who sign and date the written consent document.
 - Non-therapeutic clinical trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled.

- The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.
- The foreseeable risks to the participants are low.
- The negative impact on the participant's well-being is minimized and low.
- The clinical trial is not prohibited by law.
- The opinion of the IRB is expressly sought on the inclusion of such participants, and the written opinion covers this aspect.
- Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

References

Title VII of the Civil Rights Act of 1964 and Pregnancy Discrimination Act of 1978

45 CFR 46 Subpart B, C, D

45 CFR 46.206(a)(2)

45 CFR 46.207

40 CFR 26 Subparts C and D