# Research Involving Women of Childbearing Potential, Pregnant Women and Fetuses

## 1 Introduction and Background

### 1.1 Women as subjects of research

Historically, in order to avoid harm to a developing fetus in an unsuspected pregnancy, women of childbearing potential have been excluded from biomedical research. For example, 1977 FDA Guidelines exclude women of childbearing potential from early phase drug trials. In the late 1980s and early 1990s, recognizing that as a consequence of this "protection", women were being denied the benefits of research, women's groups began advocating strongly for expanded access. In 1988, the FDA issued guidelines that called for safety and efficacy profiles for women as part of all new drug applications, and in 1993, eliminated restrictions on women of childbearing potential participating in all phases of drug development. In 1994, the NIH issued guidelines requiring the inclusion of women in research. The NIH concluded that the only justification for exclusion of non-pregnant women of childbearing potential was compelling evidence that inclusion would be inappropriate with respect to the health of the subjects, or to the purpose of the research.

### 1.2 Pregnant women and fetuses as subjects of research

Since the 1930s, biomedical researchers in the US have used ex utero fetal tissue as an object of experimentation, including production and testing of vaccines, propagation of human viruses and testing of biological products. The 1954 Nobel Prize for Medicine was awarded to researchers who utilized human fetal kidney tissue cell lines to grow poliovirus in culture. In the early 1970s, however, the great societal debate over Roe v. Wade prompted Congress to

charge the newly established National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research to report on research using the human fetus.

The Commission report, submitted in July 1975, formed the basis for DHHS (then DHEW) regulations 45 CFR 46 subpart B (Additional Protections Pertaining to Research, Development, and Related Activities Involving Fetuses, Pregnant Women, and Human In Vitro Fertilization). In 2001 DHHS issued modifications to subpart B, now entitled “Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research”.

## 2 Research Involving Pregnant Women or Fetuses (46.204)

Subpart B generally allows research involving pregnant women or fetuses only if appropriate studies on animals and non-pregnant individuals have been completed. In addition, if the research is not intended to meet the health needs of the mother or the fetus, the risk to the fetus must be minimal. Subpart B does not give specific guidance regarding the definition of "minimal risk" in this context. In any case, the risk to the fetus must be minimized to the greatest extent possible.

To minimize the possibility that involvement in research will influence a mother’s decision to terminate a pregnancy, subpart B also excludes investigators from any decisions as to the timing, methods or procedures used to terminate a pregnancy, or determining the viability of the fetus at the termination of the pregnancy. Research involving pregnant women and fetuses may be conducted only if consent is obtained from the mother, or from both parents, after she/they have been fully informed regarding the possible impact of the research on the fetus. If the research has the prospect of direct benefit to the mother or has minimal risk to the fetus, only the mother’s consent is needed. If the research has the prospect of direct benefit only to the fetus then consent of both the mother and father are required. The father’s informed consent also need not be secured if his identity or whereabouts cannot reasonably be ascertained, he is not reasonably available, or the pregnancy resulted from rape or incest.

Click here to see Appendix for details on the requirement of maternal consent.

## 3 Research Involving Neonates (46.205)

After a fetus is delivered, it is termed a neonate (newborn). Neonates of uncertain viability, or non-viable neonates may also be subjects of research regulated by subpart B. Viability is defined as the ability of the fetus to survive, given the benefit of available medical therapy, to the point of independently maintaining heart beat and respiration. Using this definition, it is clear that "viability" is a moving target.

Neonates of uncertain viability may be involved in research only if there is no added risk to the fetus, or the purpose of the research is to enhance the possibility of survival of the particular fetus to the point of viability. Consent of legally competent mother or father, or either parent's legally authorized representative is needed.

If a fetus is determined to be non-viable after delivery, it may only be involved in research if the vital functions of the fetus will not be artificially maintained, no experimental activities which of themselves would terminate the heartbeat or respiration of the fetus will be employed, there will be no additional risk to the neonate and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means. Consent of legally competent mother and father is needed.

If a fetus is determined to be viable after delivery it is a child, and research involving that viable newborn is governed by subpart D (Additional Protections for Children as Research Subjects).

## 4 Research Involving the Dead Fetus, Fetal Material, or the Placenta (46.206)

Subpart B does not directly regulate research involving the dead fetus, stating only that these research activities shall be conducted in accordance with any applicable Federal, State or local laws. In most states the use of tissue from dead fetuses for research purposes would fall under the Uniform Anatomical Gift Act (UAGA), which requires consent of parents. However, some states specifically ban research that involves aborted fetuses, or their organs, tissues or remains.

Research involving fetal material for transplantation, and utilizing embryos produced by in vitro fertilization for the generation of human embryonic stem cell lines have been subject to additional restrictions.