Published in final edited form as:

J Med Ethics. 2012 January ; 38(1): 43–47. doi:10.1136/jme.2011.043661.

Abortion Decisions as Inclusion and Exclusion Criteria in Research Involving Pregnant Women and Fetuses

Carson Strong, Ph.D.

Department of Medicine University of Tennessee Health Science Center 956 Court Avenue, Suite G212 Memphis TN 38163 U.S.A.

Abstract

From the perspective of investigators conducting research involving pregnant women and fetuses, a woman's decision about whether to have an abortion can sometimes be relevant to the suitability of the woman and fetus as research subjects. However, prominent ethicists disagree over whether it is permissible for a woman's decision about abortion to be an inclusion or exclusion criterion for participation in research. A widely-held view is that fetuses to be aborted and fetuses to be carried to term should be treated equally as research subjects. Some hold that this principle implies that a woman's decision about whether to have an abortion should not be an inclusion or exclusion criterion. This paper identifies types of research in which investigators might want to have inclusion or exclusion criteria based on decisions about abortion. It examines the arguments for and against having the woman's decision about abortion as such criteria. It is argued that there are types of research in which such criteria are ethically permissible.

Keywords

abortion; research ethics; prenatal research; fetus; *in utero* gene transfer

INTRODUCTION

In research involving pregnant women and fetuses, is it ethically permissible for the woman's decision for or against abortion to be an inclusion criterion for entry into a study? This question has been addressed by a number of authors, and because of their differing views, it is apparent that the issue is controversial.

It is important to consider this question because of its relevance to various types of research involving pregnant women and fetuses. For example, there is growing interest in research involving administration of pharmacologic agents during pregnancy to treat diseases of either the pregnant woman or fetus.[1] Also worth mentioning is a type of research that is likely to occur in the future; namely, *in utero* gene transfer that will aim to learn how to correct certain genetic diseases prior to birth. There is growing interest in prenatal gene therapy, for several reasons.[2] First, some genetic diseases begin to have pathological effects even before birth; examples include severe combined immunodeficiency and alpha-thalassemia. For some diseases, like alpha-thalassemia, postnatal gene therapy would occur too late to reverse these harmful effects. Second, during early gestation the fetal immune system is undeveloped, and it is hoped that there is a window during which vectors carrying normal genes can be introduced without being rejected by an immune response. Given these

cstrong@uthsc.edu (phone) 901-448-5726 (fax) 901-448-2965.

Competing Interest: None declared.

potential advantages, various diseases are being considered for *in utero* gene transfer research, including hemophilia, cystic fibrosis, muscular dystrophy, and sickle cell anemia, among others.[3] Animal research currently is under way, aiming at future clinical trials.

WHY HAVE ABORTION DECISIONS AS INCLUSION AND EXCLUSION CRITERIA?

There are several reasons why investigators might want the woman's decision for or against abortion to be an inclusion criterion for a research protocol. Consider the following research scenarios:

Scenario A: A research protocol aims to evaluate the long-term outcome of a prenatal intervention that has a prospect of direct benefit to the fetus and the child into which it would develop. The investigators want to avoid recruiting women who plan to abort because pregnancy termination would preclude long-term follow up.

In this scenario, investigators might want to have as an inclusion criterion that the woman has a firm intention to carry the pregnancy to term. Examples could include Phase II studies of pharmacologic agents or gene transfer aiming to treat fetal diseases; assessments of the efficacy of the intervention would require follow up after birth. Also, in gene transfer research, adverse events could include gene alterations that lead to cancer[4] or toxic effects associated with the new gene being carried to locations other than the targeted tissue.[2,3] It might take time for these adverse effects to appear, and long term follow up would be needed to identify them.

Scenario B: A Phase I research project involves *in utero* interventions that have greater than minimal risk and hold out little prospect of direct benefit to the fetus. There is a risk of harming fetuses to be carried to term, with consequent injury to the children into which the fetuses will develop. Such injuries can be avoided by restricting the research to pregnancies planned for termination.

Adverse risk-benefit ratios of this sort would arise in Phase I research that involves *in utero* interventions such as needle insertions. Risks associated with such interventions include preterm delivery, fetal trauma or bleeding, and spontaneous abortion.[6] Preterm delivery carries risks of adverse outcomes, including cerebral palsy, chronic lung disease, and cognitive impairment, among others. When these adverse events materialize, the result is a handicapped child. Moreover, Phase I trials typically offer little prospect of direct benefit to subjects.

Scenario C: An early phase study involves injecting the fetus with an experimental agent for the purpose of assessing the uptake of the agent in fetal organs and tissues. Autopsy following pregnancy termination would permit such examination of fetal tissue.

Examples include Phase I gene transfer studies that have as endpoints the measurement of levels of the new gene or the gene product in target tissues. In both scenarios B and C, investigators would have good reasons to want to have as an inclusion criterion that the woman has decided to terminate the pregnancy. In all three scenarios, it is to be understood that the woman's decision about abortion is made prior to any discussion of research. In this way, the abortion decision is separated from the decision about participation in research.

In this paper I attempt to identify the justifiable role, if any, that abortion decisions have as inclusion and exclusion criteria for research participation. To pursue this, I shall identify and critically examine the arguments for and against using abortion decisions as inclusion or exclusion criteria.

ARGUMENTS SUPPORTING THE PERMISSIBILITY OF ABORTION DECISIONS AS INCLUSION AND EXCLUSION CRITERIA

Let us consider the main arguments for the justifiability of having abortion decisions as inclusion criteria.^[i] First, taking into consideration Scenario A, long-term follow up will be an integral part of some research. As Doris T. Zallen noted at a meeting of the U.S. Recombinant DNA Advisory Committee (RAC), accomplishment of such follow up would be promoted by recruiting only women who have a firm intent to carry the pregnancy to term (RAC, p56).^[7] [ii] Such an inclusion criterion would reduce the likelihood of dropouts and the associated loss of efficiency in use of time and resources by investigators. Explicitly having such an inclusion criterion would also promote the informed consent of subjects, by emphasizing that the purpose of the research includes long-term follow up. Whether the woman's intent is firm can be assessed in an interview in which she is invited to discuss her intention to continue the pregnancy.

Second, for types of research that potentially are harmful to future children, Amy Patterson points out that the likelihood of such harm can be reduced by restricting the research to women who intend to abort (RAC, p55).^[7] Similarly, Robert Levine notes that the risk of preterm birth and its potential harm to a future child can be diminished through such a research design. He adds that there has been a history of innovative research in which this has been recognized as an acceptable approach:

...in the early stages of development of such techniques as amniocentesis, fetoscopy, chorionic villus biopsy, and intrauterine umbilical cord blood sampling, researchers have preferred trials performed shortly before initiation of a procedure to terminate pregnancy (Levine, p 302).^[9]

To give an example, in 1979 the Ethics Advisory Board of the U.S. Department of Health, Education, and Welfare approved a research protocol designed to test the safety of fetoscopy. In that study, the new technique of fetoscopy was carried out on pregnant women at 16 to 20 weeks gestational age who had elected to undergo abortion (Anon., p8).^[10] [iii] Another RAC member, Alexander M. Capron, agrees with the argument in question, stating:

The relevance of abortion is to avoid harm to a born person. Abortion is a relevant criterion for Phase I or even Phase II trials. If there is any harm known, it should not be passed on to a born person (RAC, p57).^[7]

Third, it can be noted that, for some types of research, the objectives cannot be achieved without examining the fetus following the *in utero* intervention. This could be done through additional transuterine interventions such as obtaining fetal blood or tissue samples, but such approaches would add to the risks of spontaneous abortion and preterm birth. Potential injury to a future child can be avoided by performing the research upon fetuses to be aborted. Robert Levine points out that research examining the fetus following *in utero* interventions is necessary for establishing proper dosages of drugs used to treat fetuses, and that failure to permit such research would exacerbate the “therapeutic orphan” problem (Levine, p. 301).^[9] [iv]

^[i]In what follows, I focus primarily on inclusion criteria. If a particular decision about abortion is an inclusion criterion, then the absence of that decision can be regarded as an exclusion criterion. Thus, in this context, the concepts of inclusion criterion and exclusion criterion are directly related.

^[ii]Zallen's comment was made during a discussion of ethical issues in prenatal gene transfer. The view in question also was stated by Karen Rothenberg (RAC, p52).^[8]

^[iii]For discussion of research involving fetuses to be aborted, see Mahoney.^[11,12] See also John C. Fletcher and Joseph D. Schulman, who discuss the development of chorionic villus sampling in research involving fetuses to be aborted (Fletcher and Schulman, p9).^[13]

^[iv]See also Mirkin.^[14]

A fourth argument has been given by Ray Noble and Charles H. Rodeck. They claim that when a gene transfer has unproven efficacy, it should not be offered as an alternative to abortion because the woman might be misled into thinking that it is a therapy. Rather, recruitment should occur “only after a decision has been made not to terminate” (Noble and Rodeck, p 226).[15] Underlying this argument is a recognition of the “therapeutic misconception”—a tendency of research participants to overestimate a study's potential for therapeutic benefit.[16–19] By separating the abortion decision from the research participation decision, investigators can avoid the therapeutic misconception's influencing the woman's decision to continue her pregnancy.

As these arguments illustrate, good reasons can be given for having abortion decisions as inclusion criteria. But we also should consider the arguments against such criteria.

ARGUMENTS AGAINST THE PERMISSIBILITY OF ABORTION DECISIONS AS INCLUSION AND EXCLUSION CRITERIA

Some who object to abortion decisions as inclusion and exclusion criteria are concerned that the woman's right to make her own decision about abortion would be infringed. For example, in a conference report by the RAC, the authors state:

...as is the case for any *in utero* intervention, the pregnant woman's decision not to have an abortion cannot be used as an inclusion criterion for participation, and she must be told that she can end her participation and decide to have an abortion at any time (RAC, p 1222).[20] [v]

The RAC statement implies that having a decision not to abort as an inclusion criterion entails that the woman's right to change her mind about abortion is infringed. In reply, there is a problem with this view that can be seen by distinguishing two interpretations of what is involved in having decisions about abortion as inclusion criteria.

Interpretation 1: The prospective subject is asked by the investigator whether she plans to continue or terminate the pregnancy. Depending on her answer, she either meets or fails to meet an inclusion criterion. If she meets the criterion, she is told that, if she enters the study, she will have a right to end her participation in the study and change her mind about termination of pregnancy at any time.

Interpretation 2: The same as Interpretation 1, except that she is *not* told that, if she enters the study, she will have a right to end her participation in the study and change her mind about termination of pregnancy at any time.

Investigators should not use Interpretation 2 because doing so would fail to make it clear to the woman that she has a right to change her mind and could thereby infringe her freedom to choose whether to have an abortion. Every commentator who has discussed abortion as an inclusion or exclusion criterion agrees that the woman should retain her right to decide about abortion. The objection seems to assume Interpretation 2, and it fails to consider Interpretation 1, which is a more reasonable way to understand the use of such inclusion criteria. That Interpretation 2 is unacceptable is no argument against Interpretation 1. In the remainder of this paper, I shall assume Interpretation 1.

A second objection is related to the first but is not based on Interpretation 2. For research of the sort described in Scenario A, it might be claimed that a woman's agreement to participate in research involving long-term follow up would put pressure on her not to change her mind about continuing the pregnancy. Also, interactions with researchers committed to having the

[v]For a similar argument, see Fletcher and Richter, p1612,[21] and Chervenak and McCullough, p13.[22]

research go forward could put pressure on the woman not to change her mind. The concern is that such pressures can be an unacceptable impediment to the woman's freedom. In reply, this concern becomes attenuated when part of the inclusion criterion is that the woman's intent to carry the pregnancy is *firm*. Participation in research would seem more likely to be an influence for women who, for example, are ambivalent about continuing the pregnancy, in comparison to those who firmly intend to carry the fetus to term. Also, the objection assumes that we should prevent people from consenting to research participation when doing so might influence other decisions they might make. Presumably, the idea is that preventing such consent would promote autonomy. But it seems that autonomy would be better promoted by permitting women to consent to such research and helping them understand in advance that doing so might influence other decisions. This suggests that, as part of the informed consent process, it should be pointed out to the woman that her decision to participate in the research might possibly influence her not to change her mind about whether to terminate pregnancy. Specific factors that could influence her decision, such as researchers' enthusiasm for their work, could be pointed out. With such considerations in mind, she can then decide for herself whether to enter the study. Also, emphasizing to the woman that she is free to withdraw from the study would help diminish the force of the objection.

A third objection was raised in the deliberations of the U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (hereafter National Commission). Leroy Walters presented a paper to the National Commission in which he proposed a principle of equal treatment, according to which fetuses to be aborted should not be exposed to research interventions that would be considered too risky for fetuses going to term (Walters, p. 8-7).[23] [vi] Walters's view would preclude research of the sort described in Scenario B. There was considerable disagreement among the commissioners over this proposed rule of equal treatment, and no consensus developed on this point (National Commission, pp. 66-7).[25]

A response to this objection was given by Commissioner Karen Lebacqz.[26] She agreed that fetuses to be aborted are vulnerable subjects, equally deserving protection from harm compared to fetuses going to term. She pointed out that the disagreement is over the meaning of equal protection. Walters had maintained that equal protection requires that *procedures* not permitted for fetuses going to term should not be permitted for fetuses to be aborted. Lebacqz disagrees, claiming the equal protection requires that the *limit of risk* should be the same for both. Some research procedures have potential complications that pose greater risks for fetuses to be carried to term than they do for fetuses to be aborted. For example, a significant risk of childhood disability would be a major concern in regard to fetuses to be carried to term, but it would not be a risk for fetuses to be aborted. Therefore, equal protection of fetuses permits some procedures on fetuses to be aborted that would not be permissible for fetuses to be carried to term. Bonnie Steinbock agrees with Lebacqz. She claims that the argument by Walters "makes no sense" because the reason for preventing potentially harmful nontherapeutic research on fetuses going to term is to protect the future child. "If the woman is going to abort, there won't be any future child, and literally no one who can be harmed or protected" (Steinbock, p. 25).[27] [vii] Based on these considerations, it is reasonable to conclude that the "procedure" interpretation of equal protection is mistaken.

[vi] Commissioner David Louisell concurred with this view.[24] Also, this opinion had previously been expressed by a U.S. National Institutes of Health study group, as noted by Fletcher and Schulman, p6.[13]

[vii] See also Grady and Denny, pp413-4.[28]

Lebacqz's argument is consistent with the U.S. federal research regulations, which do not permit a change in the limit of risk just because a fetus is to be aborted. Those regulations require that the risk to a fetus not exceed *minimal risk* in research that does not hold out a prospect of direct benefit to the fetus.[29] [viii]. I assume that research involving a fetus to be aborted would not typically offer a direct benefit to the fetus. In the event that there is no direct benefit, the minimal risk standard would apply. Because the assessment of risk can depend on whether the pregnancy will be terminated, risks that exceed minimal for fetuses to be carried to term could in some cases reasonably be regarded as minimal for fetuses to be aborted. If an Institutional Review Board judges that the risks exceed minimal, even taking into account that the woman intends to terminate pregnancy, then the research is not approvable.

A fourth objection, somewhat related to that of Walters, recognizes that risks can differ for fetuses to be aborted and fetuses going to term. Instead of focusing on risks or harms, it uses any of various concepts such as dignity, integrity, and respect. This objection holds that, to avoid an affront to the dignity or integrity of the fetus, or to the respect owed to the fetus, we should not perform procedures on fetuses to be aborted that we would not perform on fetuses to be carried to term. An observation concerning this objection is worth making; although we can identify cases in which it is reasonable to claim that there is an affront to dignity, integrity, or respect, nevertheless there is a certain amount of vagueness in the meaning of these terms. Those who put forward this argument typically do not define or analyze the terms. In reply to the objection, whether there is an affront to the dignity (integrity, respect) of the fetus would seem to depend on the nature of the research procedure. For example, a procedure that has some type of mutilating effect could reasonably be regarded as a violation of the fetus. On the other hand, performing the first experimental amniocentesis on a woman who is going to have an abortion does not seem to be an affront to the fetus. The mere fact that a research procedure is performed on women planning to abort but not on women planning to carry the pregnancy does not make the procedure disrespectful toward the fetus.

A fifth objection has been raised by Ronald Green. In discussing inclusion criteria of the sort used in Scenario B, he points out two concerns: (1) "endangering the fetus in such cases will either limit a woman's freedom to change her mind about abortion" or (2) "result in harm to the child if she should choose to continue the pregnancy to term" (Green, p. 490).[31] [ix] One need not take Green's reference to limiting a woman's freedom to imply that he is disregarding Interpretation 1. Instead, one can reasonably be concerned that participation in research with a risk of injury to a future child can put pressure on the woman not to reverse her decision to have an abortion. Furthermore, although there is data suggesting that only a small percentage of women change their minds after having decided to have an abortion,[33] nevertheless some may very well do so. To permit even a few future children to be exposed to substantial risk in order to advance knowledge goes counter to the principle of respect for persons upon which our research protections are based.

Although Green has identified serious problems, there are at least two ways to design research so as to avoid them. One approach, which was advocated by Stephen Toulmin, is to have the research intervention take place as part of a single operative procedure that will conclude with the abortion (Toulmin, pp. 10-10 - 10-11).[34] This method might be feasible for research in which there is no need for a delay between the research intervention and the

[viii]The regulations provide the following definition: "*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." [30].

[ix]See also Sugarman, pp74-5.[32]

examination of fetal tissues. On the other hand, some studies might require a longer period of time for the effects of the research intervention to appear in fetal tissue. For this category of research, the problems that Green identifies can be avoided by restricting the research to fetuses with diseases that invariably are fatal during gestation or soon after birth. The lethal condition might be one upon which the research is focused. For example, a Phase I gene transfer trial dealing with alpha thalassemia could recruit women who have decided to have an abortion because they carry a fetus with alpha thalassemia, a condition that is uniformly fatal. Alternatively, the fetus's disease might not be related to the research topic but nevertheless be lethal. Either way, a Phase I trial would not alter the fetal prognosis, and if the woman changes her mind about abortion, there will not be a living child to be injured by the research.

Moreover, the concern that endangering the fetus would limit a woman's freedom to change her mind about abortion would lose its force in the scenario in question. This is because risks--and hence danger--posed to the fetus by a research intervention can differ, depending on whether the fetus has or does not have a lethal condition. Given that the fetus has a disease that is lethal during gestation or shortly after birth, the research would provide no impetus for abortion that is not already present.

The fetus's having such a lethal condition has a bearing on the assessment of whether risks exceed minimal. Risks that exceed minimal for fetuses that have a prognosis for survival and are to be carried to term could in some cases reasonably be regarded as minimal for fetuses with a condition invariably lethal during gestation or shortly after birth. For example, a transuterine needle insertion might reasonably be regarded as not exceeding minimal risk for such fetuses.

CONCLUSION

The arguments discussed in this paper support the view that it is ethically permissible to have decisions about whether to have an abortion as inclusion criteria in the following situations:

- The research aims to evaluate the long-term outcome of an *in utero* intervention and an inclusion criterion is that the pregnant woman has a firm intention to carry the pregnancy to term.
- The research offers a therapy for the fetus that has unproven efficacy, and an inclusion criterion is that the pregnant woman has a firm intention to carry the pregnancy to term.
- The potential research benefits to the fetus would be outweighed by the risks to the fetus if the fetus had a prognosis for survival and were to be carried to term, and the inclusion criteria include that (1) the pregnant woman has decided to have an abortion and (2) the fetus has a disease that is uniformly lethal during gestation or shortly after birth.
- The research involves injecting the fetus with an experimental agent for the purpose of assessing the uptake of the agent in fetal organs and tissues, and the inclusion criteria include that (1) the pregnant woman has decided to have an abortion and (2) the fetus has a disease that is uniformly lethal during gestation or shortly after birth.
- The research involves an *in utero* intervention that takes place as part of a single operative procedure that will conclude with an abortion, and an inclusion criterion is that the pregnant woman has decided to have an abortion.

The concept of inclusion criterion under consideration requires mutual understanding between investigators and the pregnant prospective subject that she continues to have a right to make her own decision about abortion. It is also required that the woman's decision about abortion is to have been made prior to any discussion of the research. Furthermore, the informed consent process should point out to the woman that participation in the research could put pressure on her not to change her decision about whether to continue the pregnancy. To be clear, it is not being claimed that all research in the above situations is justifiable, for research may be impermissible on grounds other than those pertaining to inclusion criteria. Rather, I have argued that, for research that is otherwise permissible, the inclusion criteria in question are permissible in the situations described above. The main objections to having abortion decisions as inclusion and exclusion criteria have been considered, and none of them is successful when applied to these situations.

Acknowledgments

Research for this paper was supported by grant number R03HG005225 from the National Human Genome Research Institute. The content of this paper is solely the responsibility of the author and does not necessarily represent the official views of the National Human Genome Research Institute or the National Institutes of Health. The author thanks the anonymous reviewers of an earlier draft of this paper for their helpful comments.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article (if accepted) to be published in JME editions and any other BMJ PGL products to exploit all subsidiary rights, as set out in our licence (<http://group.bmj.com/products/journals/instructions-for-authors/license-forms>).

REFERENCES

1. Mattison D, Zajicek A. Gaps in knowledge in treating pregnant women. *Gend Med*. 2006; 3:169–182. [PubMed: 17081950]
2. Coutelle C, Rodeck C. On the scientific and ethical issues of fetal somatic gene therapy. *Gene Ther*. 2002; 9:670–3. [PubMed: 12032684]
3. Waddington SN, Kramer MG, Hernandez-Alcoceba R, et al. *In utero* gene therapy: Current challenges and perspectives. *Mol Ther*. 2005; 11:661–76. [PubMed: 15851005]
4. Hacein-Bey-Abina S, von Kalle C, Schmidt M, et al. LMO2-associated clonal T cell proliferation in two patients after gene therapy for SCID-X1. *Science*. 2003; 302:415–9. [PubMed: 14564000]
5. Blakemore, KJ. [accessed 24 Feb 2011] Assessment of fetal and maternal risk; Recombinant DNA Advisory Committee. Prenatal Gene Transfer: Scientific, Medical, and Ethical Issues. 1999. p. 89-93. <http://oba.od.nih.gov/oba/rac/gtpcreport.pdf>
6. [accessed 26 Feb 2011] Recombinant DNA Advisory Committee. Minutes of Meeting. Dec 1–2. 1994 <http://oba.od.nih.gov/oba/rac/minutes/121-294.pdf>
7. [accessed 26 Feb 2011] Recombinant DNA Advisory Committee. Minutes of Meeting. Dec 4–5. 1995 <http://oba.od.nih.gov/oba/rac/minutes/124-5-95.pdf>
8. Levine, R. Ethics and Regulation of Clinical Research. 2nd ed.. Yale University Press; New Haven, CT: 1988.
9. Ethics advisory board approves waivers for fetoscopy research. *IRB*. 1979; 1(2):8. Anon.
10. Mahoney MJ. Implications of restrictions on fetal research for biomedical advance. *Clin Res*. 1975; 23:229–32. [PubMed: 10273054]
11. Mahoney, MJ. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Research on the Fetus, Appendix*. U.S. Department of Health, Education, and Welfare; Bethesda, MD: 1975. The nature and extent of research involving living human fetuses; p. 1-1.p. 1-48.DHEW Publication No. (OS) 76-127
12. Fletcher JC, Schulman JD. Fetal research: The state of the question. *Hastings Cent Rep*. 1985; 15(2):6–12. [PubMed: 4008241]

14. Mirkin BL. Impact of public policy on the development of drugs for pregnant women and children. *Clin Res*. 1975; 23:233–7. [PubMed: 10237297]
15. Noble R, Rodeck CH. Ethical considerations of fetal therapy. *Best Pract Res Clin Obstet Gynaecol*. 2008; 22:219–31. [PubMed: 17892972]
16. Appelbaum PS, Roth LH, Lidz CW, et al. False hopes and best data: Consent to research and the therapeutic misconception. *Hast Cent Rep*. 1987; 17(2):20–4.
17. Daugherty C, Ratain MJ, Grochowski E, et al. Perceptions of cancer patients and their physicians involved in Phase I trials. *J Clin Oncol*. 1995; 13:1062–72. 1995. [PubMed: 7738612]
18. Glannon W. Phase I oncology trials: Why the therapeutic misconception will not go away. *J Med Ethics*. 2006; 32:252–5. [PubMed: 16648272]
19. Meropol NJ, Weinfurt KP, Burnett CB, et al. Perceptions of patients and physicians regarding Phase I cancer clinical trials: Implications for physician-patient communication. *J Clin Oncol*. 2003; 21:2589–96. 2003. [PubMed: 12829680]
20. Recombinant DNA Advisory Committee. Prenatal gene transfer: Scientific, medical, and ethical issues. *Hum Gene Ther*. 2000; 11:1211–29. [PubMed: 11660775]
21. Fletcher JC, Richter G. Human fetal gene therapy: Moral and ethical questions. *Hum Gene Ther*. 1996; 7:1605–14. [PubMed: 8864761]
22. Chervenak FA, McCullough LB. A comprehensive ethical framework for fetal research and its application to fetal surgery for spina bifida. *Am J Obstet Gynecol*. 2002; 187:10–4. [PubMed: 12114882]
23. Walters, L. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Research on the Fetus: Appendix*. U.S. Department of Health, Education, and Welfare; Bethesda, MD: 1975. Ethical and public policy issues in fetal research; p. 8-1.p. 8-18.DHEW Publication No. (OS) 76–127
24. Louisell, DW. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Research on the Fetus: Report and Recommendations*. U.S. Department of Health, Education, and Welfare; Bethesda, MD: 1975. Dissenting statement of Commissioner David W. Louisell; p. 77-82.DHEW Publication No. (OS) 76–127
25. Research on the Fetus: Report and Recommendations. U.S. Department of Health, Education, and Welfare; Bethesda, MD: 1975. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. DHEW Publication No. (OS) 76–127
26. Lebacqz K. Fetal research: A commissioner's reflection. *IRB*. 1979; 1(4):7–8.
27. Steinbock, B. Institute of Medicine. Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies. Vol. vol. 2. 1994. Ethical issues related to the inclusion of pregnant women in clinical trials; p. 23-28.<http://www.nap.edu/openbook/0309050405/html/23.html>
28. Grady, C.; Denny, C. Research Involving Women. In: Emanuel, EJ.; Grady, C.; Crouch, RA., et al., editors. *The Oxford Textbook of Clinical Research Ethics*. Oxford University Press; New York, NY: 2008. p. 407-22.
29. U.S. Code of Federal Regulations, Title 45, Section 46.204(b).
30. U.S. Code of Federal Regulations, Title 45, Section 46.102(i).
31. Green, RM. Research with fetuses, embryos, and stem cells. In: Emanuel, EJ.; Grady, C.; Crouch, RA., et al., editors. *The Oxford Textbook of Clinical Research Ethics*. Oxford University Press; New York, NY: 2008. p. 488-99.
32. Sugarman, J. [accessed 24 Feb 2011] Ethical questions related to the prospect of *in utero* gene transfer experiments; Recombinant DNA Advisory Committee. Prenatal Gene Transfer: Scientific, Medical, and Ethical Issues. 1999. p. 71-5.<http://oba.od.nih.gov/oba/rac/gtpcreport.pdf>
33. Bracken, MB. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Research on the Fetus: Appendix*. U.S. Department of Health, Education, and Welfare; Bethesda, MD: 1975. The stability of the decision to seek induced abortion; p. 16-1.p. 16-23.DHEW Publication No. (OS) 76–127
34. Toulmin, S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Research on the Fetus: Appendix*. U.S. Department of Health, Education,

and Welfare; Bethesda, MD: 1975. Fetal experimentation: Moral issues and institutional controls; p. 10-1.p. 10-26.DHEW Publication No. (OS) 76-127