Office of Human Research Protection
Institutional Review Board
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GUIDANCE – REVIEWING VULNERABLE POPULATION STUDIES

This guidance document should be used to make determinations on studies involving children, pregnant women, fetuses, or neonates.

Section I: Studies Involving Children, 45CFR46, Subpart D	
45CFR46.404 **Research not involving greater than minimal risk.** **one parent required for consent*	A) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
45CFR46.405 **Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.** **one parent required for consent*	A) The risk is justified by the anticipated benefit to the subjects. B) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches. C) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
45CFR46.406 **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 disease or condition.** **both parents are required for consent unless meeting criteria set forth in CFR46.408(b)*	A) The risk presents a minor increase over minimal risk. B) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations. C) The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition, which is of vital importance for the understanding or amelioration of the subject's disorder or condition. D) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
45CFR46.407 **Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.** **both parents are required for consent unless meeting criteria set forth in CFR46.408(b)*	A) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children. B) The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (e.g. science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either: 1) That the research satisfies the conditions of 46.404, 46.405 or 46.406, or 2) The following: i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children. ii) The research will be conducted in accordance with sound, ethical principles. iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

Section II: Studies Involving Pregnant Women, Fetuses or Neonates, 45CFR46, Subpart B	
45CFR46.204 **Research involving pregnant women or fetuses.** **consent must be obtained in accordance with 45CFR46.204(d-g)*	Pregnant women or fetuses may be involved in research if all of the following conditions are met: 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 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 of this part; 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.
45CFR46.205 **Research involving neonates.** **one parent required for consent for neonates of uncertain viability, except as set forth in 45CFR46(b)(2); both parents required for consent for*	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.

nonviable neonates, except as set forth in 45CFR46.206(c)(5)	2) Each individual providing consent under paragraph (b)(2) or (c)(5) of this section 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 paragraph (b) or (c) of this section have been met as applicable. B) Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart 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 legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest. C) Nonviable neonates. After delivery nonviable neonate may not be involved in research covered by this subpart 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 subpart A of this part, 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 to meet the requirements of this paragraph (c)(5), 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 the requirements of this paragraph (c)(5). D) 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 subparts A and D of this part.
45CFR46.206 **Research involving, after delivery, the placenta, the dead fetus or fetal material.**	A) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities. B) If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.
45CFR46.207 **Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.** **consent to be obtained in accordance with 45CFR46.207(b)(2)(iii)*	The Secretary will conduct or fund research that the IRB does not believe meets the requirements of §46.204 or §46.205 only if: A) 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 B) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either: 1) That the research in fact satisfies the conditions of §46.204, as applicable; or 2) The following: i) 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; ii) The research will be conducted in accord with sound ethical principles; and iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.