Title: **Vulnerable Populations - Inclusion of Pregnant Women, Fetuses and Neonates in Research**	*Applicable to: **Beaumont Health**	Effective Date: **03/20/2018**
		Last Periodic Review Date: **03/20/2018**
Policy Owner: **Administrative Director**	Document Type: **Policy**	Functional Area: **IRB and Clinical Research, Research Institute**

***For This Document, Beaumont Health Includes**:
Beaumont Corporate Shared Services
Beaumont Hospital, Dearborn
Beaumont Hospital, Farmington Hills
Beaumont Hospital, Grosse Pointe
Beaumont Hospital, Royal Oak
Beaumont Hospital, Taylor
Beaumont Hospital, Trenton
Beaumont Hospital, Troy
Beaumont Hospital, Wayne
Beaumont Medical Group
Beaumont Pharmacy Solutions
Post Acute Care

I. PURPOSE:

The purpose of this policy is to provide guidance for the inclusion or exclusion of pregnant women, fetuses, and neonates from clinical research activities at Beaumont Health. **The Beaumont Health (Beaumont) IRB serves as the primary Institutional Review Board for human participant research conducted at Beaumont (for information about the use of external IRB's, see policy *Review by an External Institutional Review Board*).**

II. SCOPE:

This policy applies to investigators, key research personnel, Institutional Review Board (IRB) members and IRB staff.

III. BACKGROUND:

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.
Federal regulations address issues concerning the inclusion of pregnant women, fetuses and neonates in clinical research. These regulations are clear when the protocol offers the possibility of saving a woman's life, but offer more general guidance in other circumstances. The regulations

also state the decision to participate in clinical research is the woman's, but the father's consent should be obtained in certain circumstances.

Research involving pregnant women, fetuses, or neonates, requires the IRB to follow Subpart B of the Department of Health and Human Services (HHS) regulations.

The Beaumont IRB serves as the primary IRB for human participant research conducted at Beaumont. (Refer to IRB policy *Review by an External Institutional Review Board*, for additional information.) In accordance with federal regulations, IRB review and approval is required to protect the rights and welfare of human subjects.

IV. DEFINITIONS:

A. Pregnancy - The period of time from confirmation of implantation, as evidenced by any presumptive sign of pregnancy (e.g., missed menses, medically acceptable pregnancy test) until delivery.

B. Fetus - The unborn product of conception from the time of implantation in the womb until delivery or extraction.

C. Delivery - The complete separation of the fetus from the mother by expulsion, extraction or any other means.

D. Neonate - Newborn; from the time of birth through the first 4 weeks of life.

E. Viable Neonate - Neonate capable of surviving, given the benefit of available medical therapy, to the point of independently maintaining heartbeat and respiration.

F. Nonviable Neonate - Neonate after a live delivery, that is not viable despite medical therapy and is unable to independently maintain a heartbeat and respiration.

G. Dead Fetus - Fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

H. Macerated (fetal) Materials - Fetal materials which are broken down by extended exposure to wetness or moisture, as in a post-term infant or a dead fetus because of prolonged exposure to the amniotic fluid.

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V. POLICY:

It is the policy of Beaumont to protect the rights of all patients participating in research, including those who may be pregnant, unborn or newborn. The IRB must review all human participant research involving pregnant women, fetuses, *in vitro* fertilization and neonates. The benefits, risks, and discomforts present in the proposed research must be considered in conjunction with the expected benefits to the mother and fetus/child-participant. All viable neonates are considered children, and any research involving neonates must be conducted in compliance with IRB policy *Vulnerable Populations: Children as Research Participants*.

It is the responsibility of the individuals obtaining informed consent and conducting the research to assure the potential risks and benefits are clearly relayed to the participant or the participant's legal authorized representative (LAR). It is also important for special attention be paid to the medical condition of the participant throughout the trial in order to identify unexpected adverse events or increased risk to the participant because of his/her vulnerable condition. Research key personnel must make appropriate accommodations throughout the study to ensure continued protections of the participants' rights.

A. **Inclusion of Pregnant Women in Clinical Research Studies -** The automatic exclusion of pregnant women (i.e., without a stated rationale) is not acceptable. The principal investigator (PI) must provide a scientifically justifiable explanation of the rationale for a general inclusion or exclusion of pregnant women in a research study. A pregnant woman may not be excluded from a clinical research protocol if there is even a remote possibility of saving her life and other equivalent therapeutic alternatives do not exist.

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

   1. The purpose of the research activity is to meet the health needs of the mother, and the risk to the fetus will only be the minimum 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 mother and the fetus must be considered in the context of available alternatives.

B. **Research involving pregnant women or fetuses (in utero) may be conducted when the following conditions are met:**
   1. Scientifically appropriate studies on animals and non-pregnant women have been conducted and data provided for assessing potential risks to pregnant women and fetuses;

2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus;
3. If there is no benefit to the fetus, the risk 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;
4. Any risk to the fetus is the least possible for achieving the objectives of the research;
5. Research investigators are excluded from any decisions regarding timing, methods or procedures used to terminate a pregnancy, or determining fetal viability at the termination of the pregnancy;
6. No procedural changes which may cause greater than minimal risk to the fetus or pregnant woman will be introduced into the procedure for terminating the pregnancy solely in the interests of the research;
7. No inducements, monetary or otherwise, have or will be offered to terminate the pregnancy for research purposes.

C. **Research involving neonates of uncertain viability may be conducted when the following conditions are met:**
   1. Scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
   2. Consenting individuals have been fully informed regarding the reasonably foreseeable impact of the research on the neonate;
   3. Individuals involved in the research will have no part in determining the viability of the neonates;
   4. 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;
   5. There will be no added risk to the neonate as a result of the research activity and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means.

D. **Research involving nonviable neonates may be conducted when the following conditions are met:**
   1. Vital functions of the neonate will not be artificially maintained;
   2. The research will not terminate neonates' heartbeat or respiration;
   3. There will be no added risk to the neonate as a result of the research;
   4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

VI. INFORMED CONSENT AND AUTHORIZATION:

A. Once it has been determined pregnant women may be included in a research protocol, the decision to participate is the mother's. Consent will be obtained from the mother, or mother and father if applicable, only after she/they have been fully informed regarding the possible impact of the research on the fetus or neonate.

Informed consent and authorization will be required from the mother only, (not the father) in the following circumstances:

1. The research has the prospect of direct benefit to the pregnant woman.
2. The research has the prospect of direct benefit to both the pregnant woman and the fetus.
3. The research has no direct benefit to either the pregnant 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 through other means.

B. When the **pregnant woman is a minor, assent from the minor and permission from the pregnant minor's parent(s) must be obtained** under the guidance provided in IRB policy *Vulnerable Populations: Children as Research Participants*. The pregnant minor is allowed to consent for research for her fetus or neonate.

C. **Informed consent is required of both the pregnant woman and the father if the research holds out the prospect of direct benefit solely to the fetus**, unless the father is deceased, unknown, incompetent, not reasonably available or if the pregnancy resulted from rape or incest.

D. **In research involving neonates of uncertain viability, consent may be obtained from either parent**. If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's LAR may be obtained.

E. **Research involving nonviable neonates may be conducted only if the mother and father are legally competent and have both given their consent.** The father's consent need not be obtained if the pregnancy resulted from rape or incest. Additionally, 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. The consent of a LAR of either or both parents will not suffice for research involving a nonviable neonate.

For research after delivery involving the placenta, the **dead fetus or fetal material** when information associated with the material is recorded in a manner that living individuals can

be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and afforded all protections under 45 CFR 46.

F. **For research involving a viable neonate where there is greater than minimal risk and no prospect for direct benefit to the neonate, but research is likely to yield generalizable knowledge about the subject's disorder, both parents must give their consent** unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. The father's consent need not be obtained if the pregnancy resulted from rape or incest.

The mother and father of a fetus or neonate must be legally competent in order for an informed consent to be valid. If the father's consent is required, his signature should be added to the informed consent and authorization document; if not, the basis for the exception should be noted on the informed consent and authorization document.

G. **Research Involving or Supported by the Department of Defense (DoD) -** For purposes of applying Subpart B, the phrase "biomedical knowledge" shall be replaced with "generalizable knowledge." The applicability of Subpart B is limited to research involving pregnant women as participants which is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as subjects. Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

H. **Recruitment of Pregnant Women, Neonates and or Fetuses –** When promotional material mentions Beaumont, references a Beaumont department (e.g., Urology Research) or Beaumont physician, or provides a Beaumont phone number, Marketing approval is required. If the promotional material is targeted towards enrollment of pregnant women, neonates and/or fetuses the promotional material needs to pay particular attention to being non-coercive in nature. Additionally, the requirements of the *Clinical Research Study Promotion policy* and the *Compensation and Incentives Offered to Research Participants* policy must be followed. Prospective IRB review and approval of marketing materials is required prior to use in any study related activity.

VII. REFERENCES:

21 CFR 50 Subpart B Informed Consent Requirements
21 CFR 50 Subpart D Additional Safeguards for Children in Clinical Investigations
45 CFR 46 Subpart B Additional Protections for Pregnant Women, Human Fetuses, and Neonates

45 CFR 46 Subpart D Additional Protections for Children Involved as Subjects in Research
45 CFR 46.116 Requirements for Informed Consent
45 CFR 46.117 Documentation of Informed Consent
IRB Informed Consent and Authorization Template
IRB Assent Template

VIII. ASSOCIATED POLICIES:

IRB policy *IRB Initial Review of Research Protocols*
IRB policy *Informed Consent and Authorization in Research*
IRB policy *Vulnerable Populations: Children as Research Participants*
IRB policy *Review by an External Institutional Review Board*
IRB Policy *Clinical Research Study Promotion*
IRB Policy *Recruiting Human Participants for Clinical Research*
Founding Beaumont Patient Care Policy 304 *Informed Consent*
Founding Oakwood Policy 1005 *Informed Consent Policy and Process for Verification of Informed Consent for Surgical/Medical and Other Procedures*
Founding Botsford Policy C118P *Consent Policy, Informed*

CORPORATE AUTHORITY:

Beaumont Health ("BH") as the corporate parent to William Beaumont Hospital, Botsford General Hospital, and Oakwood Healthcare Inc., ("Subsidiary Hospitals") establishes the standards for all policies related to the clinical, administrative and financial operations of the Subsidiary Hospitals. The Subsidiary Hospitals, which hold all health facility and agency licenses according to Michigan law, are the covered entities and the providers of health care services under the corporate direction of BH. The Subsidiary Hospitals' workforces are collectively designated as BH workforce throughout BH policies.

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