Title: **Vulnerable Populations: Children as Research Participants**	*Applicable to: **Beaumont Health**	Effective Date: **03/19/2018** Last Periodic Review Date: **03/19/2018**
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 define "children/minors" as it applies to the federal regulations and describe the oversight required for children to be enrolled in human participant research at Beaumont Health (Beaumont). The IRB of record for Beaumont research may be the Beaumont IRB or an approved external IRB, in accordance with IRB policy *Review by an External Institutional Review Board*.

II. SCOPE:

This policy applies to Beaumont investigators, key research personnel and IRB members.

III. BACKGROUND:

Children are recognized as a special and vulnerable population. To safeguard their interest and protect them from harm, special ethical and regulatory considerations apply when involving children in research. The IRB will comply with all applicable regulations and guidelines to assure the rights and welfare of these study participants are protected.

IV. DEFINITIONS:

A. **Assent** - A child's affirmative agreement to participate in research. Failure to object should not be construed as assent.

B. **Benefit** - A valued or desired outcome; an advantage.

C. **Children (minors) -** Persons who are less than 18 years of age. In Michigan, the legal age for consent is 18 years of age.

D. **Dissent** - A person's negative expressions, verbal and/or non-verbal, which reveals an objection to participation in the research or research activities.

E. **Emancipated Minor** - A legal status conferred upon persons less than 18 years of age, for whom a parent is no longer legally responsible, which occurs in the following instances: a minor who is legally married; the period during which a minor is on active duty with the U.S. Armed Forces; for the purpose of consenting to routine, non-surgical medical care or emergency care when the minor is in the custody of a law enforcement agency and the minors parent or guardian cannot be promptly located; upon entry of an emancipation order by the Circuit Court.

F. **Guardian -** An individual who is authorized under State or local law to consent on behalf of a child to general medical care.

G. **Greater than Minimal Risk** - The probability and magnitude of harm or discomfort anticipated in the research is greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

H. **Legally Authorized Representative -** An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research activities. For an un-emancipated minor child, a parent or an individual *in loco parentis* (in the position or place of a parent) may consent if there is no legal guardian or other court-appointed representative or if the legal guardian or court-appointed representative is unavailable act. In addition, an adult sibling of a minor may consent if the parent or person acting *in loco parentis* is not available to act.

I. **Minimal Risk -** 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. Example: drawing a small amount of blood from a healthy individual for research purposes (the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).

J. **Parent** - A child's biological or adoptive parent.

K. **Risk** - The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant.

V. POLICY:

It is the policy of Beaumont to protect the rights of all persons participating in research, including children. The IRB must review all human participant research involving children. The benefits, risks, and discomforts present in the proposed research must be considered in conjunction with the expected benefits to the child-participant, other children with the same disease or condition, or to society as a whole. The IRB will not approve any research involving children which does not qualify for approval under the federal regulations.

Research involving children is subject to the Health and Human Services regulations Subpart D. The IRB follows the requirements of Subpart D for research involving children. Subpart D requires IRB review of some research activities involving children that would be exempt if the research participants were adults. The scope of exemption is reduced when the participants are children. The exemption of research activities involving survey and interview procedures is eliminated for child-participants. Also, the exemption is narrowed for research involving observations of public behavior, by eliminating the exemption of any research involving observation of public behavior if the investigator will participate in the activities being observed when child-participants are involved.

A. **Minimal versus Greater than Minimal Risk Procedures -** Procedures presenting no more than minimal risk to a healthy child include, but are not limited to, urinalyses, obtaining small blood samples, EEGs, EKGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests. However, the probability and magnitude of risk in sick children may be different, depending on the diseases or conditions affecting the child. Therefore, assessing risk is done on a case-by-case basis by the IRB. Examples of

procedures considered greater than minimal risk include, but are not limited to, biopsy of internal organs, spinals taps, or use of drugs or devices whose risks to children have not yet been established.

The IRB assessment of possible benefits of research participation for children will consider the health status of potential participants (e.g., healthy, sick, early stage disease, end stage disease), and the likelihood of disease progression without research intervention.

B. **Categories of Risk -** The IRB must classify research involving children into one of three categories as part of its review process. These categories are based on the degree of risk and benefit to individual participants.

1. **Category 1. Research does not involve greater than minimal risk to children (21 CFR 50.51, 45 CFR 46.404).** When the IRB finds there is no greater than minimal risk to children present, the IRB may approve the research only if adequate provisions are made for soliciting the assent of the children and permission of their parent(s) or legal guardians. The IRB determines whether the permission of one or both parents is required 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.
2. **Category 2. Research involves greater than minimal risk, but presents the prospect of direct benefit to the individual child (21 CFR 50.52. 45 CFR 46.405).** If the IRB finds more than minimal risk to children is presented by an intervention or procedure offering the prospect of direct benefit for the individual child, or by a monitoring procedure likely to contribute to the child's well-being, the IRB may approve the research if it finds:
   a. The risk is justified by the anticipated benefit to the children; and
   b. The relation of the anticipated benefit to the risk is at least as favorable to the children as that present in currently available alternative approaches; and
   c. Adequate provisions are made for soliciting the assent of the children and permission of their parent(s) or legal guardians. The IRB determines whether the permission of one or both parents is required 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.
3. **Category 3. Research involving greater than minimal risk and no prospect of direct benefit to the individual child, but is likely to yield generalizable knowledge about the disorder or condition (21 CFR 50.53, 45 CFR 46.406).** If the IRB finds more than minimal risk to children is presented by an intervention or procedure that does not hold

out the prospect of direct benefit for the individual child, or by a monitoring procedure which is not likely to contribute to the well-being of the child, the IRB may approve the research if it finds:

a. The risk represents a minor increase over minimal risk; and
b. The intervention or procedure presents experiences to participants reasonably equal to those who are part of their actual or expected medical, dental, psychological, social or educational situations; and
c. The intervention or procedure is likely to yield generalizable knowledge about the disorder or condition, which is of vital importance for the understanding or improvement of the disorder or condition; and
d. Adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians. For research that involves more than minimal risk without the prospect of direct benefit to the individual children, the IRB determines the permission of both parents is required 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.

If the IRB determines the research protocol does not meet the criteria for Category 1, 2 or 3 and believes the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, the proposed protocol may be sent for review by the Commissioner of the Food and Drug Administration (FDA) and/or the Secretary of the Department of Health and Human Services (21 CFR 50.54, 45 CFR 46.407).

C. **Informed Consent/Assent Process -**Research which includes children as participants most often will require permission of the parent(s) or guardian and the assent of the child. Permission must be documented in the medical and research records in accordance with federal regulations. In Category 1 or Category 2 research, the IRB may determine the permission of only one parent (or the guardian) is required, if consistent with laws/regulations in the jurisdiction in which the research is conducted. The circumstance for obtaining only one signature must be documented in the IRB application and the IRB meeting minutes. In some cases, such as research involving the study of child abuse or sexually transmitted disease, the IRB may determine parental permission is not required.

D. **Written Parental Permission** - Adequate provisions must be made for soliciting the permission of each child's parent(s) or legally authorized representative (LAR).
Note: Court Appointed Guardians must present a letter from the Court to authenticate the Guardianship.

The requirements vary per degree of risk inherent to the research:

1. **For minimal risk research studies (Category 1):** The written permission (i.e., signed informed consent and authorization form) of **one** parent/guardian is sufficient.* Children should give assent as appropriate.
2. **For research involving greater than minimal risk, but with a potential of benefit to the participant (Category 2):** The written permission (i.e., signed informed consent and authorization form) of **one** parent/guardian is sufficient.* Children should give assent as appropriate.
   ** Consent of both parents may be necessary depending on the custodial relationship of the parents.*
3. **For research involving greater than minimal risk and with no prospect of direct benefit to the child (Category 3): Both** parents must give written permission (i.e., signed informed consent and authorization form) unless one parent is deceased, unknown, incompetent, or not reasonably available, or only one parent has the legal responsibility for the care and custody of the child. Children should give assent as appropriate**.**

E. **Waiver of Parental Permission Documentation - For minimal risk research studies (Category 1):** The IRB may approve a procedure waiving the requirement for obtaining a parent's signature on the informed consent and authorization document if:

1. The research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research study; AND
2. The research is not pertaining to the FDA regulations.

In cases in which the informed consent and authorization documentation requirement is waived by the IRB, key personnel may be required by the IRB to provide participants with a written statement regarding the research called an information sheet. When the Beaumont IRB is IRB of record, rather than an approved external IRB, alterations or waivers to the informed consent and authorization process are requested by completing the appropriate fields in the IRB application in iMedRIS, the electronic submission system

F. **Waiver of Parental or Legal Guardian Permission -** If the IRB determines a research study is designed for conditions or a participant population for which parental or LAR permission is not a reasonable requirement to protect the participants (e.g., neglected or abused children), they may waive the consent requirements. In order to protect the rights and welfare of the children, the involvement of a court appointed guardian may be considered.

The requirement for parental permission may be inappropriate in cases involving older adolescents who, under applicable law, may consent on their own behalf for selected treatments (e.g., treatment for drug abuse, emotional disorders, and sexually transmitted diseases) and for research which is not FDA-regulated.

The waiver must be consistent with Federal, State, or local law, and an appropriate substitute mechanism for protecting the minor participants must be in place, e.g., a social worker or child advocate.

G. **Obtaining Assent -** For each study, the IRB determines and documents whether assent is a requirement of: a) all children, b) some children, or c) none of the children. When the IRB determines assent is not a requirement of *some* children, the IRB will determine and document which children are not required to assent.

When the IRB determines assent is not a requirement for *some or all* children, the IRB will determine and document one or more of the following:

1. The children are not capable of providing assent based on the age, maturity, or psychological state.
2. The capability of the children is so limited they cannot reasonably be consulted.
3. The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research.
4. Assent can be waived using the criteria for waiver of the consent process.

Adequate provisions must be made for soliciting the assent of minor participants when, in the judgment of the IRB, the children are capable of providing assent. In making this determination, the IRB takes into account the ages, maturity, and psychological state of the children involved. This judgment may be made globally for all children as potential participants in a particular research study, or individually for each child. The child should be given an explanation of the proposed research procedures in a language appropriate to the child's age, experience, maturity, and condition. This explanation should include a discussion of any discomforts and inconveniences the child may experience if he or she agrees to participate.

While children may be legally incapable of giving informed consent, they may have the ability to assent to or dissent from research participation. Out of respect for children as developing persons, children should be asked whether or not they wish to take part in the research, particularly if the research does not involve interventions likely to benefit participants, and the child is capable of comprehending the meaning of volunteering for the

benefit of others. **As an ethical standard, the IRB recommends verbal assent be obtained from children ages 7 through 13 years and written assent obtained from children ages 14 through 17 years.** The consent provider providing assent of the minor must utilize their judgment to assess the child's reading level of understanding. If a child is able to read at a young age, the younger age child (7-13 years) may also receive the written assent document, in addition to providing verbal assent.

H. **Waiver of Assent** - If the IRB determines either of the following to be true, obtaining assent from the minor participant may **not** be necessary:
   1. The capability of some or all of the children is so limited they cannot reasonably be consulted; **or**
   2. The intervention or procedure involved in the research holds the prospect of direct benefit that is important to the health or well-being of the child and is only available through the research. In such circumstances, a child's dissent (which should normally be respected), may be overruled by the child's parents, at the IRB's discretion; **or**
   3. The interventions or procedures involved in the research hold prospect of success and the probability of discomfort is high. In such cases, parents may feel compelled to exhaust all available interventions, including all available experimental options. If the child does not wish to undertake such experimental therapy, the IRB will deliberate carefully. Generally, if the child is a mature adolescent and death is imminent, the child's wishes will be respected.
   4. Even where the IRB determines the child participants are capable of assenting, the IRB may waive the assent requirement under circumstances in which consent may be waived for adults.

I. **Emancipated Minors -** Under Michigan law, there are no conditions under which a child below the age of 16 years can be considered emancipated. Children 16 years of age or older may be emancipated under the following circumstances:

   Without a court order only **one** of the following need apply:
   1. When a minor is married; or
   2. When a minor is on duty with the US armed forces; or
   3. For the purposes of consenting to routine non-surgical medical care or emergency medical treatment when a minor is in the custody of a law enforcement agency and the minor's parents or guardian cannot be located; or
   4. For purposes of consenting to his/her own preventative health care or medical care including surgery, dental care, or mental health care, except vasectomies or any procedure related to reproduction, during the period when the minor is a prisoner or a

probationer residing in a special alternative incarceration act, but only if the parent or guardian cannot be located by the Department of Corrections.

By Court Order: The court will issue an emancipation order if it determines emancipation is in the best interest of the minor and the minor is able to establish **all** of the following:

1. The minor's parent or guardian does not object to the emancipation or if the parent or guardian does object, the parent or guardian is not supporting the minor; and
2. The minor is at least 16 years of age; and
3. The minor is a Michigan resident; and
4. The minor has demonstrated the ability to manage his or her financial affairs, including proof of employment or other means of support; and
5. The minor has the ability to manage his/her personal and social affairs, including but not limited to housing; and
6. The minor understands his/her rights under the act as an emancipated minor.

J. **Wards of the State** - Children who are wards of the state or any other agency, institution, or entity can be included in research only if the research is:

1. Related to the child's status as a ward; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

The IRB requires appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or *in loco parentis*:

1. The advocate is an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research.
2. The advocate is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization

K. **IRB Submission -** When enrolling children into research, it is necessary to address the risk category level (Category 1, 2 or 3) of the protocol and the parental permission and assent requirements. When the Beaumont IRB serves as IRB of record, as opposed to an approved external IRB, this is addressed in the reviewer checklist and IRB minutes.

For children ages 8-13, the Informed Consent and Authorization Form should have a signature line for verbal assent to be signed by the person obtaining the assent. A script or outline of the content of the verbal assent must be submitted along with the IRB protocol submission.

For children ages 14-17, written assent must be obtained from the participant utilizing a document written at an appropriate reading level. If the reading level of the Informed Consent and Authorization form is appropriate for children ages 14-17, then it is acceptable to add a signature line for the child's written assent and use the one form for both child and parent(s). A separate written assent form may be required if the language in the Informed Consent and Authorization document is too complex for the child to understand.

L. When **promotional material** names Beaumont, references a Beaumont department (e.g., Pediatrics Research), Beaumont physician, or provides a Beaumont phone number, Marketing approval is required. If the promotional material is targeted towards children, the materials must be age appropriate for the study populations' understanding. Requirements of the *Clinical Research Study Promotion* policy and the *Compensation and Incentives Offered to Research Participants* policy must also be followed. Prospective IRB approval of all research related promotional materials is required.

M. **Investigator Responsibilities -** The PI must make the initial determination of the appropriate Category (1, 2, or 3) in which the research falls, and provide justification in the IRB initial submission for this determination. The protocol should describe if, and how, assent and dissent will be obtained and documented.

The PI must take into account the ages, maturity, and psychological state of the children. In general, a child's dissent should be respected. Every effort should be made to reach consensus between parent and child, however, when the research offers the child the possibility of direct benefit important to his/her own health and is available only through research, the parents' wishes generally prevail.

The investigator or authorized consent provider may only approach the child to consent or assent to the research study after the parents or legal guardians **have given written permission (unless the IRB has waived the requirement.** The consent provider providing consent or assent of the minor must utilize their judgment to assess the child's understanding level. If a child is able to read at a young age, the younger age child (8-13) may also receive the assent for written requirements to be applied.

N. **Research Involving or Supported by the Department of Defense (DoD) -** DoD research involving children cannot be exempt.

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VI. 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 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

VII. ASSOCIATED POLICIES:

IRB policy *IRB Initial Review of Research Protocols*
IRB policy Informed Consent and Authorization in Research
IRB Policy Clinical Research Study Promotion
IRB Policy Compensation and Incentives Offered to Research Participants
IRB Policy Review by an External Institutional Review Board
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.