INSTITUTIONAL POLICY & PROCEDURE
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TITLE:
Institutional Review Board Special Considerations
SC 501 Children as Research Participants

ORIGINATOR:
Institutional Official

APPROVAL:
Institutional Official

POLICY STATEMENT: The purpose of this document is to detail the requirements for Institutional Review Board (IRB) approval of research involving children as human subjects. Children are considered to be a vulnerable population, and therefore must be treated with special consideration. In addition to the protection provided under the Common Rule (45 CFR 46), federal regulations provide additional protections for children involved in research such as obtaining consent from the child and permission from the parents/guardians. Research involving viable neonates also must comply with the additional regulatory protections for children. Also, in addition to federal regulations, all research conducted at Mercy Health regional sites complies with the CHE Trinity Health Mission, Core Values, and Catholic moral/ethical principles, as delineated in the "Ethical and Religious Directives for Catholic Health Care Services." In this regard, IRB review and decision making gives special consideration for research participants' cultural, racial, social, religious, and economic circumstances.

GENERAL PROVISIONS:
The special vulnerability of children makes consideration of involving them as research subjects particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations are in place for reviewing research involving children. Research that is contrary to the rights and welfare of child-subjects is prohibited. The IRB must take great care in approving research where the child is suffering from a life-threatening illness with little real chance of therapeutic benefit from the research. The IRB must also be cautious in allowing parents to overrule a child’s dissent where experimental therapy has little or no reasonable expectation of benefit.

Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted", 45 CFR 46.402(a).

The IRB review of research involving children as subjects will consider the benefits, risks, and discomforts inherent in the proposed research and assess their justification in light of the expected benefits to the child-subject or to society as a whole. In calculating the degree of risk and benefit, the IRB will weigh the circumstances of the subjects under study, the magnitude of risks that may accrue from the research procedures, and the potential benefits the research may provide to the subjects or class of subjects.

Criteria for Approval
Research involving children qualifies for Exemptions at 45 CFR 46.101(b)(1) and (b)(3) through (b)(6). Exemptions at 45 CFR 46.101 (b)(2) apply when regarding educational tests, but it does not apply for research involving survey or interview procedures or observations of public behavior unless investigators do not participate in the activities being observed.

If a study does not qualify for an exemption, the IRB should approve research only if it finds the following criteria from 45 CFR 46, Subpart D:
A. Risk level must be determined and categorized as follows:
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- Research not involving greater than minimal risk.
- Research involving greater than minimal risk but presenting the prospect of direct benefits to the individual subjects.
  - The risk is justified by the anticipated benefit to the subjects;
  - The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches
  - Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408.

B. 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 disorder or condition.

C. Research not otherwise approvable which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children.

Determination of probable risks and associated discomforts: Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests. The assessment of the probability and magnitude of the risk, however, may be different in sick children and may vary depending on the diseases or conditions the participants may have. For example, obtaining blood samples from a hemophiliac child may present more than minimal risk to the child. On the other hand, IRBs may consider that children suffering from chronic illnesses who are accustomed to invasive procedures are placed at minimal risk by involvement in similar research procedures, in contrast to children who have not had such experiences. The IRB must also consider the extent to which research procedures would be a burden to any child, regardless of whether the child is accustomed to the proposed procedures.

Procedures that exceed the limits of minimal risk may be difficult to define in the abstract, but should not be too difficult to identify on a case-by-case basis. Riskier procedures might include biopsy of internal organs, spinal taps, or the use of drugs whose risks to children have not yet been established. Behavioral interventions likely to cause psychological stress may also exceed minimal risk.

Determination of possible benefits: In assessing the possible benefits of research intervention, the IRB should consider the variability in health statuses among potential participants. For example, a potential subject might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (e.g., meningococcus or lead) where it is known that a percentage of the children exposed will actually experience untoward consequences. A child may also be in an early state of disease, e.g., an HIV-infected child, or may actually suffer from disease or other significant medical condition. Thus, the IRB must take into account the current health status of a child and the likelihood of progression to a worsened state without research intervention.

B. Consent Requirements

a. Requirements for permission by parents or guardians and for assent by children.
   i. Both parent signatures are required unless the research study involves minimal risk or more than minimal risk but presents the prospect of direct benefits to the individual subjects. In this case, a waiver of parental signature may be granted.
   ii. Both parents are required to give permission if research involves greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject’s disorder or condition, or research not otherwise approvable but presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children.
   iii. Parental/guardian permission may be waived if the IRB determines it is not a reasonable requirement and if a waiver is allowable by federal, state, or local law.
   iv. If parental/guardian permission is waived, the IRB must substitute an appropriate mechanism to protect the children acting as subjects. Substitute will be determined depending on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

b. Assent: The IRB must account for ages, maturity and psychological state of the children involved to determine if they are capable of assenting. The IRB can determine if assent standards apply to every child involved in the protocol, or if assent should be individually based for all the children involved in the protocol.
   i. Assent is not necessary if IRB determines that the child does not have the ability to understand what he or she is asked.
   ii. Assent is not necessary if IRB determines that a child will only receive a direct benefit from being a subject in human research.
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DOCUMENTATION OF CONSENT
In addition to either an Exempt or Standard Application, investigators must submit consent documentation for IRB review. Consent for research involving children is a two-fold process. It requires consent from two different groups: children and their parents.

Assent: All children must give assent before research procedures begin unless there is prospect for direct benefit then parental permission is sufficient. The IRB should look for age appropriate questions investigators will ask children in order to obtain assent. These questions include the following:

- What will constitute assent denied?
- What will constitute assent given?
- How can the child withdraw assent?
- How will you introduce yourself?
- How will you engage the child?
- How will you invite the child?
- How will you tell the child about the research activity?

Parental Permission: If parent or guardian permission is required, Investigators must provide a Parent Permission Form informing parents of the procedures, risk, privacy, possible benefits, etc. of the research study. Investigators cannot begin research procedures until the informed consent discussion takes place and the Parent Permission Forms are fully signed. Parent Permission Forms must be submitted to the IRB for review.

Waiver of Consent: If parent permission is unavailable or unnecessary, a Request for Waiver of Informed Consent must be submitted.

WARDS
A. Children who are wards of the state or any other agency, entity or institution can only act as research subjects if research is:
   a. Related to their status as wards; or
   b. Conducted in schools, camps, hospitals, institutions or similar settings in which the majority of children involved as subjects are not wards.

B. Advocates
   - An advocate must be appointed for wards acting as subjects, as well as any other individual acting on behalf of the child as guardian or in loco parentis.
   - One individual may serve as advocate for more than one child.
   - The advocate shall be an individual who has the background and experience, as well as agrees to act in the best interests of the child for the duration of the child’s participation in the research.
   - The advocate cannot be associated in any way with the research, the investigator(s) or the guardian organization.

EMANCIPATION
Emancipation alters the legal status of a minor, rendering the minor an adult for all intents and purposes. In order to petition for emancipation, a minor must meet the requirements of the state that they reside and file for petition for emancipation with the court. The effect of a final decree of emancipation is that the child has the same right to make contracts, etc as if they were an adult.

It should be noted that solely becoming a parent is NOT enough for a minor to establish his/her ability to give consent for themselves.

DEFINITIONS: The following definitions are referenced in 45 CFR 46.402:
- Children: Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
  a. The state of Michigan defines children as persons less than 18 years old.
  b. If a child outside of the State of Michigan participates as a human subject in Michigan, the IRB will seek legal counsel regarding special review considerations.
- Assent: A child’s affirmative agreement to participate in research. Mere failure to object should not be construed as assent.
- Permission: Agreement of parent(s) or guardian to the participation of their child or ward in research.
- Parent: A child’s biological or adoptive parent.
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- Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

REFERENCES:
45 CFR 46.101
45 CFR 46, Subpart D
45 CFR 46.402

ATTACHMENTS:
SC 501 A-Assent Template
SC 501 B- Requirements for Research Involving Children (Worksheet)

PROCEDURE: All Mercy Health Campuses

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<th>Responsibility</th>
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<tr>
<td>IRB Specialist/IRB Coordinator</td>
<td>1) Confirm that study submission has informed consent and assent documents as appropriate</td>
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<td>2) Provide a full submission package with the appropriate checklist/worksheet to the IRB Chairperson for review</td>
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<td>3) Issue IRB Letters as advised by the IRB Chairperson</td>
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| IRB Chairperson                 | 1) Review the submission package or item to determine if adequate materials exist for review of the criteria for approval to allow children to participate in the study. |
|                                 | 2) Notify the IRB Specialist of the need to place the item on the next IRB Meeting agenda if a full committee review is required. |
|                                 | 3) Notify the IRB Specialist of any expedited review and approval of the submission package when appropriate. |
|                                 | 4) Notify the IRB Specialist of the review outcome and request issuance of appropriate IRB letter. |

| IRB Assigned Reviewer           | 1) Complete the Worksheet for Research Involving Children. Return written concerns/comments to the IRB Specialist for review within the requested timeframe. |

| Investigator                    | 1. Create plan for assenting of children as outlined in this policy and conduct assent and consent as approved by the IRB. |

| IRB Members                     | 1. Review all studies involving children taking into account the additional regulations set forth by the FDA and OHRP. |
|                                 | 2. Ensure children are assented when appropriate. |
|                                 | 3. Ensure content of assent is appropriate for the children's age range. |

CONCURRENT CONSENTS:

Institutional Official

Version Date 05/04/2015