Institutional Review Board Procedure No. 25

EFFECTIVE DATE: ***March 25, 2022***

PROCEDURE TITLE:

Vulnerable Populations: Children

To be reviewed every three years by:
Institutional Review Board

REVIEW BY: ***March 24, 2025***

PROCEDURE

This Procedure implements the requirements of Institutional Review Board Policy No. 1 *Authority of the Institutional Review Board*, which requires the Trinity Health Mid-Atlantic (THMA) Institutional Review Board (IRB) establish policies and procedures to ensure that the THMA's IRB operations fully comply with applicable laws, regulations, professional standards, and the *Ethical and Religious Directives for Catholic Health Care Services*, including promoting the conduct of ethical and compliant research.

When children are included in research, the IRB will ensure that the research meets all children regulations.

Application

All research that involves children must meet all of regulatory criteria whether one child or several children are to be enrolled in the study and regardless of whether children are the target of enrollment or not. When a study was not initially approved for the enrollment of children, but a researcher later wishes to enroll one or more children, the Investigator must first submit a revision to the IRB and gain approval by full board prior to enrolling any children.

Definition of a Child

Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable jurisdiction in which the research will be conducted. In Pennsylvania, Delaware, and Maryland the legal age for consent is 18 years of age unless the child has been emancipated.

I. IRB Review of Research with Children

A. IRB Membership

The composition of the IRB membership must have representation to include the professional expertise necessary to consider children as research participants. There are four main issues to consider when reviewing research involving children: (a) justification for the

use of children in research, (b) risk-benefit analysis; (c) parental permission [informed consent obtained from the parent(s)]; and (d) assent of the child. These are discussed below:

B. Justification for the Use of Children in Research

When an IRB considers research that involves children, the IRB should determine whether the study has or can be performed using a less vulnerable population, such as adults. The IRB should also consider whether healthy children could be used, rather than sick children, if applicable. The justification for the use of children in research should be reflected in the IRB minutes.

C. Risk/Benefit Analysis

IRBs must make risk/benefit and other determinations when reviewing research involving children and the IRB minutes must reflect the IRB's understanding and justification for the risks and benefits posed by research involving children. The IRB must consider whether additional safeguards are needed based, in part, upon the presence or absence of direct benefit and the justification for acceptable risk. To aid in this framework, the proposed research must fall within one of the following four categories:

1) Research not involving greater than minimal risk.
2) Research involving greater than minimal risk, but presenting the prospect of direct benefit to the child or a monitoring procedure that is likely to contribute to the child's well-being (such as ambulatory EEG monitoring or other intracranial monitoring for a child with chronic epilepsy, a continuous glucose monitor for a child with diabetes, etc.)
3) Research involving greater than minimal risk and no prospect of direct benefit to the child, but likely to yield generalizable knowledge about the child's disorder or condition.
4) Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

Each of these four categories further contains specific criteria for approval which must be met and which are provided in detailed in Table 1.

Research that involves children suffering from a life-threatening illness with little real chance of therapeutic benefit from the research is not typically conducted at THMA. There are additional requirements that must be met to approve this type of research which also includes involving the Commissioner of the FDA and a panel of experts. Contact the THMA IRB if there are plans to conduct this type of research.

The IRB will determine and document the Pediatric Risk Level for each new proposed research protocol and ensure that all of the criteria are met, in the IRB meeting minutes. The category and Pediatric Risk Level determinations are indicated in the initial approval letter to the principal investigator for the study being reviewed and approved. During the course of the study the IRB may determine that a pediatric risk level has changed to due unforeseen events. This change will be documented at the time of review in the IRB meeting minutes and communicated in a letter to the principal investigator.

D. Parental Permission

1. Obtaining

Parental permission, by way of informed consent, is required when children are involved in research. The number of parental signatures is determined by the level of risk of the study, as reflected in Table 1, after this policy.

2. Waiving

- Parental permission may not be waived for a FDA regulated study, except for emergency use of a test article or planned emergency research. See THMA IRB policy: Emergency Use of a Test Article.
- Parental permission (consent) may typically be waived for non-FDA regulated studies if certain regulatory criteria are met (Common Rule regulated studies).

FDA-regulated research means: a clinical investigation that is supported by or subject to the oversight of the FDA. Generally, these are investigations that support applications to prove safety and efficacy or marketing permits for products regulated by the FDA (including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products).

Common Rule, DHHS and OHRP regulated research means: All research subject to oversight of the Department of Health and Human Services (DHHS), or OHRP.
Contact the IRB Administrator for assistance with the definitions.

Research studies that are subject to oversight of OHRP or DHHS regulations must meet the criteria for waiving parental consent. The criteria are:

a) the research involves no more than minimal risk;
b) the waiver will not adversely affect the parental' rights and welfare;
c) the research could not practicably be carried out without the waiver; and
d) when appropriate, the parents will be provided with pertinent information after participation.

If the THMA IRB determines that the research study is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the children (for example, neglected or abused children), the IRB may waive the consent requirements, provided that:

1. an appropriate mechanism for protecting the children who will participate in the research is substituted, and
2. the waiver is not inconsistent with federal, state, local law, or tribal law.

The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the research study, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition.

Parental permission may not be waived for studies that involve elementary and secondary school children for non-emergency, invasive physical examinations and for surveys

involving certain protected information (political affiliations or beliefs of student or parent, mental and psychological problems of student or family, sexual behavior or attitudes, illegal, anti-social, self-incriminating, or demeaning behavior, etc.).

E. Assent from the Child

1. Definition

Assent is a child's affirmative agreement to participate in a research study. A child's assent (or dissent) is to be honored. A child's refusal should be respected at all times and especially when the proposed intervention is not essential to the child's welfare.

2. Capacity to Assent

In addition to ensuring parental permission (consent), the IRB must determine whether (a) the child is capable of assenting and (b) that adequate provisions are made for soliciting the assent of each child who is being considered for participation in research. In determining when children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the child participants involved. This judgment may be made for all of the children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate.

3. Not Obtaining or Waiving Assent

Not a Necessary Condition:

The assent of the children is not a necessary condition for proceeding with the research if the IRB determines:

a. That the capability of some or all of the children is so limited that they cannot reasonably be consulted, or
b. That the intervention or procedure involved in the clinical investigation holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the clinical investigation.

Not Obtaining or Waiving Assent:

Even where the IRB determines that the child is capable of assenting, the IRB may determine that assent will not be obtained under one of two regulatory mechanisms:

a. The first regulatory option is that when 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 children and is available only in the context of the research, the child's assent is not a necessary requirement to proceed with the research.
b. The second regulatory option is to waive the assent requirement where:
    i. the research involves no more than minimal risk;
    ii. the waiver will not adversely affect the child's rights and welfare;
    iii. the research could not practicably be carried out without the waiver; and
    iv. when appropriate, the child (and parents) will be provided with pertinent information after participation.

Please note that when the IRB waives or does not require the child’s assent in a study, the parents’ permission is still required.

4. Obtaining and Documenting Assent

When the IRB determines that some or all of the children are capable of assenting, then the IRB must next determine if the assent should be read to the children and/or provided in writing to the children, and if so, whether documentation (signature of the child) should be required. The written assent document or verbal script must be at an appropriate reading level for the children.

When the THMA IRB determines that assent is required, it must also determine whether and how assent must be documented. The emphasis on obtaining assent should be on the interactive process in which information and values are shared and joint decisions are made. Pictures may sometimes be used to help illustrate a procedure or short video may be shown. The assent form, if used, is just one piece of the assent process.

a. **Children ages 7-17-Written assent is typically used:**
   The written assent document may differ in language and presentation of content to target specific age groups (teenagers vs younger age ranges). For young children, the assent form should be a relatively brief document, with simple, age-appropriate language, presented in a manner understandable to the child. For older children, the assent should still be brief and appropriate to their level of reading.
b. **Children ages 7-17- Requiring the child's signature (documentation of assent) is typically used:** Although federal regulations do not stipulate a particular age range for providing documented assent of children (signature), the age range of seven years of age or older has typically been used in the clinical research setting.
c. **Children below the age of 7- Verbal script read and/or no signature typically used:**
   The Investigator should submit all applicable documents: verbal script, written assent document, whether or not they will obtain a signature from the child and the age ranges for each scenario. When the IRB determines that some or all of the children are not required to sign the assent document, this will be reflected in the meeting minutes and in writing to the investigator. When the IRB determines that some of all of the children may be assented by using a verbal script, this too will be documented in the IRB minutes and in writing to the investigator.

Each research proposal is reviewed by the IRB with the mindset that the assent process should be one that considers not only age but also other characteristics of the target population as it relates to the risk/benefit of the objective to be studied. Most importantly, the assent process should provide ample opportunity for children to express and discuss their willingness or unwillingness to participate, regardless of whether written assent is conducted.

All and any assent documents, story boards, oral scripts, videos must be reviewed and approved by the IRB before they can be utilized in approved research endeavors.

II. Children who are Wards

Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 (risk level 3 or level 4) only if such research is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

The use of children who are wards should be considered carefully by the IRB and alternatives should be considered first, such as adults or children who are not wards. Additional safeguards should be considered for the children who are wards in the research.

When a research study meets the above criteria, the THMA IRB shall require 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. One individual may serve as advocate for more than one child. The advocate shall be 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 and who 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.

III. Definitions

- **Children (Minors)** – persons who are less than 18 years of age unless the child has been emancipated.
- **Assent** – the child's affirmative agreement to participate in the research. Mere absence of an objection should not be construed as assent.
- **Parental Permission** – the agreement of parent(s) or guardian to the participation of the child or ward in the research. Investigators need to obtain permission for the child to be enrolled in the research project by way of a parental consent document.
- **Guardian** – an individual who is authorized under state, local law, or tribal law to give permission on behalf of a child to general medical care. Although other relatives (i.e. grandparents, siblings) may give consent for clinical care when they have custody of a child without legal authority, they may not give permission for research studies. If the researcher wishes to enroll a child under a research project, the researcher must seek permission from the parents, legally appointed guardian, or have the court appoint another relative as the legal guardian.
- **Parent** – a child's biological or adoptive parent. If a foster parent provides documentation that establishes guardianship then the foster parent may be considered a legal guardian.
- **Minimal Risk** – means that the research participant will not experience any harm or discomfort than ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- **Emancipated** – a legal status where upon persons have reached the age of 18 or by virtue of assuming adult responsibility; such as marriage or serving on active duty in the military or be virtue of a court order.
- **Ward** –a minor who by reason of incapacity (as a minor) is under the protection of a court either directly or through a guardian appointed by the court—called also ward of court.

TABLE I
Categories of Research and Pediatric Risk Levels

Risk of Harm Category	Requirements
Level I (45 CFR 46.404 & 21 CFR 50.51) **No greater than minimal risk, with or without potential for direct benefit to the child.**	Assent* of child and permission** of at least one parent/ guardian.
Level II (45 CFR 46.405 & 21 CFR 50.52) **Greater than minimal risk and prospect of direct benefit to the child or a monitoring procedure that is likely to contribute to the child's well-being.**	Assent* of child and permission** of at least one parent/ guardian.
	Anticipated benefit justifies the risk
	Anticipated benefit is at least as favorable as that of available alternative approaches
Level III (45 CFR 46.406 & 21 CFR 50.53) **Greater than minimal risk and no prospect of direct benefit to the child, but likely to yield generalizable knowledge about the child's disorder or condition.**	Assent* of child and permission** of both parents/guardians Both parents must give their permission 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.
	Only a minor increase over minimal risk
	Likely to yield generalizable knowledge about the child's disorder or condition that is of vital importance for the understanding or amelioration of the disorder or condition
	The intervention or procedure presents experiences to the child that is reasonably commensurate with those in the child's actual or expected medical, dental, psychological, social, or educational situations.
Level IV (45 CFR 46.407 & 21 CFR 50.54) **Research not otherwise approvable (does not meet the requirements of Level I, II, or III).**	Assent* of child and permission** of both parents/guardians Both parents must give their permission 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.
	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 children
	The HHS Secretary or the FDA Commissioner approves, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following publication in the Federal Register and public comment. See Final Guidance "Process for Handling Referrals to FDA under 21 CFR 50.54 – Additional Safeguards for Children in Clinical Investigations-December 2006

NOTE: * Assent can be waived by the IRB ** Parental/Guardian Permission = Parental Informed Consent

RESPONSIBLE DEPARTMENT

Further guidance concerning this Procedure may be obtained from the Trinity Health Mid-Atlantic Institutional Review Board.

Effective Date: March 25, 2022

Subsequent Review/Revision(s):