The Christ Hospital IRB
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(II.3.A, II.3.F, II.4.A, II.4.B)

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STANDARD OPERATING PROCEDURE

Additional Protections for Children Involved as Subjects in Research

POLICY:

The Christ Hospital requires that research will include additional safeguards to protect the rights and welfare of subjects when some or all of the subjects are children. In addition to its other prescribed responsibilities, the IRB will review research involving children and approve only research which satisfies the applicable conditions as set out below. All research involving children, regardless of funding source, will be reviewed and approved in accordance with 45 CFR Part 46, Subpart D, as applicable.

Definitions:

Children are 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.

Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.

Parent means a child's biological or adoptive parent.

Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

I. Research involving Children (45 CFR 46.401)
Children may be involved in research if all the conditions listed in 45 CFR 46.401 are satisfied:

I. Research not involving greater than minimal risk. 45 CFR 46.404

a) IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.

II. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. 45 CFR 46.405

a) IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a

monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:

i. The risk is justified by the anticipated benefit to the subjects;

ii. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and

iii. 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.

III. 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. 45 CFR 46.406

a) IRB finds that 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 subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

i. The risk represents a minor increase over minimal risk;
ii. 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;
iii. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
iv. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408.

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

For HHS-funded research, if the IRB believes the research does not meet the review requirements or conditions of 45 CFR 46.404, 45 CFR 46.405 or 45 CFR 46.406, but 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;, then the research will be referred to OHRP in accordance with 45 CFR 46.207. For non-HHS-funded research, the IRB may approve the research if it finds that the research will be conducted in accordance with sound ethical principles and informed consent will be obtained in accordance with the informed consent provisions of 45 CFR 46, including all applicable subparts.

V. Requirements for permission by parents or guardians and for assent by children. 45 CFR 46.408

i. In addition the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for

all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that 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 assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with 45 CFR 46.116 of Subpart A.

ii. In addition to the determinations required, the IRB shall determine, in accordance with and to the extent that consent is required by 45 CFR 46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404 or 45 CFR 46.405. Where research is covered by 45 CFR 46.406 and 45 CFR 46.407 and permission is to be obtained from parents, 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.

iii. In addition to the provisions for waiver contained in 45 CFR 46.116 of Subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon 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.

iv. Permission by parents or guardians shall be documented in accordance with and to the extent required by 45 CFR 46.117 of Subpart A.

v. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

VI. Wards 45 CFR 46.409

a) Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 45 CFR 46.407 only if such research is:
   i. Related to their status as wards; or
   ii. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

b) If the research is approved under 45 CFR 46.409(a) of this section, the 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 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 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.

PROCEDURE

Investigator:

- Completes protocol submission forms, indicating children will be the target population for the research activities.
- Addresses obtaining informed consent process, assent process and selection of participants with particular attention to preventing undue influence or coercion.

IRB Chair:

- Assesses whether the protocol meets the criteria for research involving children.
- Reviews the protocol to ensure the following:
    - All required materials were submitted (See SOP 2.01, Guidelines for Protocol Submission) for Subpart A, using the IRB Review Checklist A.
    - The additional required information is provided to satisfy Subpart D for research activities involving children. Using the IRB Checklist for Children
- Contacts investigator and/or study coordinator with questions or needed clarification/documentation regarding the vulnerable population.
- Assures that the IRB discusses and makes the required determinations under 45 CFR 46.404, 405, 406, and/or 46.408, when applicable.
- For HHS-funded research that the IRB believes is not approvable under 45 CFR 46.406 but presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children.
    - Refers to the HHS Secretary through OHRP for determination on the conduct and/or funding of the research under 45 CFR 46.407.
- Verifies that discussion and determinations of the IRB are reflected in the minutes.
- Reviews the IRB minutes, including the IRB's protocol-specific findings justifying waiver of the consent process or waiver of documentation of consent.
- Issues approval only after all criteria in subparts A and D are satisfied.

IRB Staff:

- Assists IRB Chair in preparing the letter of determination to the investigator.
- Documents discussion and required determinations of the IRB in the minutes.
- Mails approval and informed consent documents.

IRB Members:

For convened IRB review, each member:

- Reviews the protocol at the time of initial or continuing review.
- Reviews the research outline assuring additional protections for chidren are included.
- Reviews the proposed research, informed consent process, assent process and other applicable documents to determine whether the study meets criteria at 45 CFR 46.111, and 21 CFR 56.111 if applicable, for approval by the convened IRB.
- Discusses the proposed research, taking into consideration additional requirements for children to participate in research described in 45 CFR 46, Subpart D.
- The IRB believes the protocol is not approvable under the criteria above, but finds the research presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, and
    - If the research is funded by HHS, refers the protocol to OHRP for a determination under 45 CFR 46.407(b); defers further action until a response is received from OHRP; reviews any changes proposed by OHRP through the response review process, and takes final action on the protocol at that time,
    - If the research is not funded by HHS, approves the research only if it determines the following are satisfied: 1) the research is conducted in accordance with sound ethical principles, and 2) informed consent will be obtained in accordance with 45 CFR 46 Subpart A and all applicable additional subparts.

    - Issues approval only when all applicable sections of 45 CFR Part 46 Subparts A and D are satisfied.