The Christ Hospital IRB
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STANDARD OPERATING PROCEDURE

Scientific/Scholarly Review of Protocols – Minimizing Risks to Subjects

POLICY:

Research involving human subjects must undergo review to ensure scientific or scholarly validity by the Principal Investigator's department and the IRB. Department chairs, and section chiefs, if applicable, are responsible for determining that proper scientific and department approvals have been obtained and that the hypothesis and procedures are consistent with generally accepted scientific principles in the discipline. The department chair approval also confirms that the PI has appropriate training and expertise, adequate resources and sufficient time allocation to conduct the research, and that the research is pertinent to the needs and goals of the institution, department and community, and has been found to be acceptable for IRB submission.

Investigators, in accordance with relevant standards of their discipline, will conduct studies using sound research design which includes minimizing risks to subjects under the requirements of this policy. Study designs should monitor subjects sufficiently to detect harm promptly. An investigator will not implement a change in the IRB approved research protocol without prior IRB approval, except to eliminate an apparent immediate hazard to a research subject. All such changes must be reported to the IRB, and FDA if applicable, within 5 working days.

The IRB is responsible for determining that the following requirements are satisfied for each research protocol reviewed (Ref: 21.CFR 56.111):

1. Risks to the subjects are minimized: a) by using procedures which are consistent with sound research technique and which do not unnecessarily expose subjects to risk, and b) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to human subjects are reasonable in relation to anticipated benefits, if any, to subjects and to the importance of the knowledge that may be expected to result.
    a. For the purpose of IRB consideration, "benefit" is defined as a valued or desired outcome; an advantage.
    b. For the purpose of IRB consideration, "risk" is defined as the probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a research study. In evaluating risk, the IRB is to consider the conditions that make this situation dangerous, per se (i.e., as opposed to those chances that specific individuals are willing to undertake for some desired goals).
    c. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (i.e., as distinguished from risks and

benefits from treatments and procedures that the patient would undergo if not participating in the research).

d. In evaluating risks and benefits, the IRB does not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within purview of its responsibility.

3. Selection of subjects is equitable. In making this assessment, TCH IRB should take into account the purposes of the research and the setting in which the research will be conducted and be particularly cognizant of the special problems of research involving vulnerable populations, such as pregnant women, handicapped or mentally disabled persons, or economically or educationally disadvantaged persons. (See Reference Manual, Section 6, for more information regarding vulnerable populations.)

4. Human research subjects are adequately informed of the risks and benefits of research participation and the procedure that will be involved in the research, and that informed consent is obtained from each prospective human research subject, or his/her legally authorized representative, in accordance with and to the extent required by federal regulations, IRB policies and state law.

5. Informed consent of human research subjects is obtained in advance of research participation and appropriately documented in accordance with and to the extent required by federal regulations (21 CFR 50.27), and IRB guidelines.

6. The research plan, when appropriate, makes adequate provision for monitoring the data collected to ensure the safety of human research subjects. Furthermore, data from monitors that may be noted to be adverse to human subjects will be promptly reported to the principal investigator and to the IRB in compliance with federal regulations and IRB guidelines.

7. There are adequate provisions to protect the privacy of human research subjects and to maintain the confidentiality of research data.

8. Appropriate additional safeguards have been included in the study to protect rights and welfare of human research subjects who are likely to be vulnerable to coercion, or undue influence (eg., pregnant women, decisionally impaired persons or economically or educationally disadvantaged persons). TCH IRB does not participate in research concerning prisoners. (See Reference Manual 6.2 for information regarding research subjects who become incarcerated.)

TCH IRB may, at its discretion, invite consultants to assist in review of issues which require expertise beyond or, in addition to, that available within the IRB. A consultant is an individual with competence in special areas. Review of research may benefit from advice by consultants in such areas as scientific knowledge of the research, experience with vulnerable populations, and knowledge of the research context among others. Whenever possible the IRB will identify consultants from within TCH or TCH-related entities. Consultants will be appointed by the IRB Chair (or designee). The IRB may authorize the Chair (or designee) to engage consultants with subsequent ratification by the IRB. Consultants will be subject to the conflicting interest rules applicable to IRB members and will not vote with the IRB. The

consultant will not be counted toward the quorum requirement.

PROCEDURE

INVESTIGATOR:

- Completes and submits appropriate IRB protocol application and applicable materials as listed on the "TCH IRB New Protocol Cover Sheet", and as outlined in SOP 2.01, "Guidelines for Protocol Submission".
- Provides enough documentation to demonstrate the methodology and procedures are consistent with generally accepted scientific principles in the discipline.
- Describes in the protocol past experimental and/or clinical findings, including those conducted by the investigator, leading to the formation of the study.
- Provides information in the protocol to support the safety of the research and includes relevant literature on safety and effectiveness of a test article when not supplied in the research protocol or Investigator's Brochure.
- Describes the study methodology that will affect the participants, particularly in regard to any inconvenience, danger or discomfort.
- Lists the procedures (including screening), the length of time each will take, and their frequency.
- Identifies procedures being performed as part of standard diagnostic or treatment procedures.
- Lists any possible physical, psychological, social, legal or economic risks associated with study procedures, their frequency, severity and reversibility.
- Describes any alternative treatments and any withholding of normal treatment.
- Describes the anticipated risk-benefit ratio and the expected knowledge to be gained by the research.
- Describes the precautions that will be taken to avoid hazards for the participants and the means to detect hazards.

DEPARTMENT CHAIR:

- Completes departmental scientific review and approval, and electronically signs in Mentor IRB.

IRB OFFICE STAFF:

- Ensures new protocol submission, progress reports or protocol modifications are complete and sufficient for IRB review.
- Verifies all required submission documents for new studies have been received.
- Verifies that the departmental scientific review and approval is complete for new studies, as applicable.
- Assigns submission requiring full board review to the Full Board Panel. This action places the protocol on the next meeting agenda for review
    - Ensures the submission documents are available in their entirety in Mentor IRB for IRB member review approximately two weeks prior to the convened meeting date.
- Assigns submission applicable for expedited review to the IRB Chair or designee for review.

- Documents, for the minutes, IRB determinations that risks are minimized and substantive discussions, as appropriate.
- Documents, for the minutes, IRB determinations of anticipated benefits, if any, and the importance of the knowledge that is expected to be gained by the research outweighs the research risks and substantive discussions, as appropriate.
- For reviews that require a consultant:
    - Distributes materials to consultants, including financial disclosure form of no conflicting interest.
    - Distributes written summary of consultant, if provided, to IRB members with convened review materials.
    - Documents in the IRB minutes key information provided by consultant during the oral presentation.
    - Attaches consultant's written summary and/or any written presentation materials to the minutes and files in the protocol record.

IRB SCIENTIFIC MEMBERS:

- The IRB Chair and a designated scientific member of the board review each protocol for scientific merit and scholarly validity with accompanying materials utilizing the New Protocol Reviewer Checklist.
- Reviews and assesses the following elements:
    - Whether the protocol and procedures are consistent with sound research design.
    - Whether the procedures do not unnecessarily expose participants to risk.
    - Whether the protocol uses procedures already being performed as part of routine diagnostic or treatment purposes, when appropriate,
    - Whether the research provides for detecting harms promptly and avoiding hazards.

If a scientific member of the IRB cannot adequately evaluate the scientific and scholarly validity of an assigned protocol:

- He/she may perform a scientific assessment through study of the relevant literature, discussions with colleagues, and contact with the principal investigator provided that the materials are received for review are kept confidential, or
- He/she notifies the Chair prior to the time the protocol is scheduled for presentation at the IRB meeting. If notified before the meeting, the Chair decides whether to review the protocol, invite a consultant to assist in the review.
- If notified at the meeting, the IRB decides whether to review the protocol at the meeting, or to table the protocol to another meeting and invite a consultant to assist in the review.
- For expedited review, the protocol is reviewed for scientific merit and scholarly validity by the IRB Chair. If unable to assess, the Chair may get a consultant review.

IRB MEMBERS:

- All IRB members review the application and informed consent document and may request a copy of the accompanying materials prior to the meeting or examine them at any time in the IRB office prior to the meeting.
- Approves the research only after assuring that:
    - Procedures are consistent with sound research design;

    - Procedures do not unnecessarily expose participants to risk; and
    - Procedures are already being performed as part of routine diagnostic or treatment purposes, when appropriate; or

- Determines whether protocol modifications are necessary to minimize risks;
- Determines whether sufficient provisions are included to promptly detect harms and avoid hazards to the research subjects, or requests modifications to include additional provisions, as needed; and
- Determines if risks are reasonable in relationship to anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected to result.

IRB CHAIR:
For expedited review of initial or continuing submissions or submissions of modifications or amendments, the IRB Chair:

- Assesses the information presented regarding risks to participants and determines that the research qualifies for expedited review under criteria for minimal risk;
- Determines if the risks are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that is expected to result;
- Documents that all criteria are met before approval; or
- In cases where the Chair is unable to make the determination, refers the protocol to the convened IRB.