The Christ Hospital IRB
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IRB REFERENCE MANUAL
SECTION 01
PREFACE: JURISDICTION, STRUCTURE AND RESPONSIBILITIES OF THE CHRIST HOSPITAL INSTITUTIONAL REVIEW BOARD

1.0 PREFACE: JURISDICTION, STRUCTURE AND RESPONSIBILITIES OF THE CHRIST HOSPITAL INSTITUTIONAL REVIEW BOARD

Vision: The Vision of The Christ Hospital is to be a national leader in clinical excellence, patient experience, and affordable care.

Mission: The Mission of The Christ Hospital is "Improve the health of our community and create patient value by providing exceptional outcomes, affordable care and the finest experiences, all in an affordable way."

The IRB is charged with responsibility for protecting human subjects and research participants.

1.1 The Institutional Review Board of The Christ Hospital

The Mission of The Christ Hospital Institutional Review Board (TCH IRB) is to facilitate research and ensure the protection of rights, privacy and welfare of all human participants who are the subjects of research.

To achieve this goal, the IRB has the authority to review, approve, modify or disapprove research protocols submitted to the IRB by investigators. The IRB will assist the investigators in designing their research projects in a manner which minimizes potential harm to human subjects, review all planned research involving human subjects prior to initiation of the research, approve research that meets established criteria for protection of human subjects, and monitor approved research to ascertain that human subjects are indeed protected. The IRB review process is guided by ethical principles outlined in the Belmont Report (1979) and legal mandates outlined in the Code of Federal Regulations Title 45 Part 46 (2005).

The Christ Hospital IRB (TCH IRB) is designated to oversee research on human subjects conducted by the administration, nursing, medical and resident staff, or involving non-public information held by Christ Hospital. The purpose of the IRB is to protect the rights and welfare of human subjects participating in research and to ensure that the human research conducted under this policy meets federal requirements [DHHS 45 CFR 46] [FDA 21 CFR 50, 56, 812] and conforms to

federal and state laws, and The Christ Hospital's policies. The ethical principles are based on the Nuremburg Code, the Declaration of Helsinki, the Belmont Report, and the International Conference on Harmonization (Good Clinical Practices).
The president/CEO of The Christ Hospital is responsible for the appointment of members of the IRB and the oversight of the TCH IRB. The Christ Hospital may not approve research covered under this policy if it has not been approved by the IRB, however, the Institutional Official may decline to conduct research previously approved by the IRB. Investigators should not begin research involving human subjects until the Christ Hospital's IRB has approved the study or has determined that it is exempt.

1.2 Other Institutions

In the absence of an authorization/reliance agreement, human subject research conducted by The Christ Hospital personnel as indicated at another institution will require review and approval by both The Christ Hospital IRB and the Institutional Review Board of the other institution. To expedite the approval process, it is recommended that approval of the external review board be obtained prior to submitting the research protocol to TCH IRB, and TCH IRB will accept the specific format and requirements of the external institution provided that the general requirements as outlined in this reference manual are appropriately addressed. If the other institution does not have an Institutional Review Board, approval of TCH IRB may be the only IRB approval requirement depending upon the nature of the activities to be conducted at the other institution, specifying that all institutional commitments and regulations, applicable laws, and standards for professional conduct in practice have been appropriately addressed by the investigators. Note: If human subject research will be conducted in or involving the staff, patients, students, etc., of an institution which has not executed a authorization agreement with The Christ Hospital IRB, and which does not have its own Institutional Review Board, the respective Christ Hospital application must include a letter from a responsible administrator of the institution indicating his/her permission for the research to be conducted at that institution.

Other institution's assurance agreements: Conduct of federally supported human subject research at another institution is subject to the requirement that the other institution have in place a Federal Wide Assurance (FWA) agreement with The U.S. Department of Health & Human Services (DHHS) Office for Human Research Protection (OHRP). If the other institution does not have an FWA in place, it may be required (i.e., depending upon the research activities to be conducted at that institution) to execute an FWA agreement with OHRP prior to the conduct of the research at that site. Contact the TCH IRB office for a clarification of this requirement as it pertains to the specific research activities to be performed at the other institution.

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1.3 Composition of the IRB

The Christ Hospital IRB is directed by a chairperson and is comprised of at least five board members with multidisciplinary expertise and backgrounds as required by federal policy and FDA regulations. In addition, the IRB office staff includes an administrator to review research studies that qualify for exempt or expedited (i.e., administrative) review status, and a regulatory specialist who assures the IRB meets federal regulations, as well as institutional policies and procedures. IRB members are covered for liability under one of the following: (1) If the member is a Christ Hospital employee, he/she is covered by the self-insured trust fund; (2) Volunteer members are covered under The Christ Hospital National Union Policy (located in the Risk Management office) which covers past, present and future members.

1.4 Appointment of the IRB

The president/CEO of The Christ Hospital will appoint IRB members, including the chairperson, in accordance with federal regulations for a non-specific term.

Members will serve without compensation, although the chair might receive compensation due to the extended duties and time requirement. The board will be multi-disciplined and comprised of at least five voting members (including the chair). Voting members will be representative of the active medical staff, a pharmacist, at least one member of scientific and one member of non-scientific discipline, and at least one community member. There will be ethnic and gender diversity. In addition, several persons will be appointed to serve in ex officio capacity without vote, such as the institutional official. Consultants may be asked to serve without vote where their particular competence would assist the consideration of the board; e.g., an attorney, clergy, social worker and medical specialists. Attendance is recorded and if a member misses a majority of meetings without substantive cause or explanation, the IRB chair will discuss the advisability of resignation with the board member and report to the institutional official.

When appointing members to the IRB, the following qualities should be considered:

a. Commitment to institutional goals for human research protections
b. Commitment to the time commitment and the workload; must be able to regularly attend IRB meetings, arrive on time and be prepared for discussion
c. Good communication skills; ability to present issues and concerns clearly and succinctly; provide other members with clearly articulated required changes to the research, if any
d. Willingness to contact investigators, IRB chair and/or administrator prior to the meeting to discuss issues and initiate solutions; use the IRB meeting to make decisions, not gather information
e. Ability to communicate with the IRB office in a timely manner if unable to attend a meeting, or if conflicts of interest will require recusal from the voting process for a particular protocol

Additional qualifications of an IRB chair include, but are not limited to:

a. Demonstrable knowledge and the ability to consistently apply the regulations governing research and the IRB review process
b. Demonstrable knowledge of The Christ Hospital's human research protection program and the ability to consistently apply IRB policies and procedures
c. Demonstrable knowledge and the ability to apply the ethical principles of human research protections
d. The ability to appropriately apply the relevant knowledge to the individual protocols under review
e. Ability to lead IRB members in a thorough review, abiding by all policies, procedures and applicable federal, state and local laws, rules and regulations

f. Demonstrable meeting management and time management skills; ability to act as a facilitator, timekeeper, summarizer and consensus taker.

1.5 Duties of IRB Members

The IRB is appointed as a TCH committee. As such, the IRB members serve The Christ Hospital as a whole, rather than a particular school or department. Therefore, members must not allow their own interests or that of their departments to supersede their duty to protect the rights and welfare of research subjects. Each IRB member's primary duty is the protection of the rights and welfare of the individual human beings serving as research subjects. The reviewer must understand that he or she is not serving on the Institutional Review Board to expedite the approval of research, but to serve as a link between the investigator and the research subjects. In order to fulfill his or her duties, each IRB member is expected to be knowledgeable of the regulations governing human subject protection, biomedical and behavioral research ethics, and the policies of The Christ Hospital germane to human subject protection. The IRB must be fair and impartial, immune to pressure by the institution's administration, the investigators bringing protocols before the board, or other professional and nonprofessional sources.

All members are expected to review and be familiar with all material, and come prepared to discuss the material at the convened IRB meeting.

Nonaffiliated members: Nonaffiliated members are expected to provide input regarding their knowledge about the local community and be willing to discuss issues and research from that perspective.

Non-scientific members: Nonscientific members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and otherwise. For example, members who are lawyers should present the legal views of specific areas that may be discussed, such as exculpatory language or state requirements regarding consent. Non-scientific members should advise the board as to whether additional expertise in a non-scientific area is required to assess whether the protocol adequately protects the rights and welfare of subjects and to comment on the comprehension of the consent document.

Scientific members: Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of practice. These members should also be able to advise the Board if additional expertise in a scientific or non-scientific area is required to assess whether the protocol adequately protects the rights and welfare of subjects.

Chairperson: In addition to the above responsibilities (germane to the member's capacity) the chairperson chairs the meetings of the IRB. The chair performs or delegates authority to an appropriate voting board member perform expedited review when appropriate. The chair is empowered to suspend the conduct of a

research project or clinical trial deemed to place individuals at unacceptable risk pending IRB review. The chair is also empowered, pending IRB review, to suspend the conduct of a study if he/she determines that an investigator is not following the IRB's policies or procedures (continuing noncompliance). The chair may appoint a co- or associate chair to assist or act on their behalf in particular IRB matters and at IRB meetings, either as a general procedure or on a case-by-case basis. The co- or associate chair requires the same qualifications as the chair. The chair also may delegate any of his/her responsibilities, as appropriate, to other qualified individual(s). Such delegation must be in writing or documented in the record of the IRB.

Primary Reviewers: The chairperson or his/her designee will act as primary reviewer at convened meetings. The primary reviewer presents his or her findings resulting from review of the application materials and provides an assessment of the soundness and safety of the protocol, and recommends specific actions to the board. He or she leads the discussion of the study by the convened IRB. The primary reviewer is required to read the entire submission, be familiar with it, and be prepared to conduct an in-depth review of all materials. The primary reviewer is expected to contact the investigator, IRB chair or IRB administrator in advance of the convened meeting for clarification of unresolved issues related to the submission.

Reporting Undue Influence: Any IRB members or TCH staff who becomes aware of an allegation of undue influence or coercion regarding IRB policies and/or procedures must report the incident(s) immediately to the IRB Chairman. The Chairman along with a selected community member of the IRB will initiate an inquiry into the allegation and initiate a report to the president/CEO of The Christ Hospital. The president/CEO will resolve the issue and notify the IRB of the outcome.

1.6 IRB Membership Roster

A roster of IRB members and alternates is created and maintained by the IRB Coordinator. The roster identifies members by:

a. Name
b. Earned degrees
c. Experience, qualifications, specialty (board certification, licenses, IRB certification)
d. Designation as Principal, Ad Hoc or Ex Officio Member
e. Scientific/non-scientific designation
f. Employment by or relationship to the IRB or other member
g. Hospital or institutional affiliation

The membership roster is reviewed at least annually by the IRB office staff and the IRB chair to assure appropriate membership and diversity as outlined in 45 CFR 46 and 21 CFR 50.

1.7 Meeting Attendance

Members are requested to attend the scheduled meetings in order to maintain their appointments to the Board. The IRB office staff will maintain an attendance log with cumulative attendance recorded on a calendar year basis for review with the IRB chair at each meeting. The chair will contact members who miss 6 consecutive meetings and determine the action to be taken. The chair may ask for the resignation of the member if deemed necessary. Unaffiliated members are expected to attend 80% of their convened IRB meetings a year. Unless there is a last-minute emergency or illness and a substitute cannot be found, there will be an unaffiliated member at every IRB meeting. The attendance of the unaffiliated members will be documented in the meeting minutes. Unaffiliated members are non-scientific members and represent the general perspective of subjects. At a meeting in which the IRB reviews research that involves subjects vulnerable to coercion or undue influence, one or more individuals who are knowledgeable about or experienced in working with such subjects must be present.

1.8 Removal of Members/Vacancies

A member, alternate, ad hoc or ex officio member (including the IRB chair) may be removed, with or without cause, from the IRB:

a. By the action of the president/CEO or institutional official of The Christ Hospital, on the recommendation of the IRB chair
b. Automatically, if the member misses 6 consecutive meetings or has a pattern of non-attendance
c. The IRB chair may resign with a one-month notice
d. A member may resign from the IRB by submitting a letter of resignation to the chair
e. Vacancies in the membership shall be filled by the appointment process following the guidelines described above (see “Appointment of the IRB”).

1.9 Quorum

Quorum shall be established with a majority of the members present, including at least one member whose primary interest is in a non-scientific area. All members of the IRB have full voting rights and a project is deemed approved with a positive vote of simple majority of those present at the meeting where quorum has been established. If quorum is lost during a meeting, the IRB cannot take votes until the quorum is restored. If required members (e.g., non-scientific members) leave the room and quorum is lost, votes cannot be taken until the quorum is restored, even if half of the members are still present. Voting by proxy is prohibited. An investigator may not cast a vote on the consideration of his/her project, and is

required to leave the meeting room during the discussion and when the vote is cast on a project in which he/she has a conflict of interest.

1.10 No Quorum Present

In the event quorum is not present, the IRB chair will cancel the meeting and schedule a make-up meeting before the beginning of the following month. The make-up meeting will ensure that all IRB protocols scheduled for continuing review can be reviewed by the expiration dates.

1.11 Purpose of IRB Review

The IRB review is to assure, both in advance and by periodic monitoring, that appropriate steps are taken to protect the rights and welfare of human research subjects, and to ensure the confidentiality of the subject's protected information. The focus of the IRB review process is outlined in Chapter 11.

1.12 IRB Staff and Responsibilities

a. Chair: Has ultimate responsibility for the review/approval of human subject research conducted under the jurisdiction of TCH IRB; evaluates each protocol and assigns a primary reviewer with appropriate scientific expertise to conduct an in-depth review of the protocol; conducts IRB meetings; reviews and approves meeting minutes; approves emergency use notification; oversees the administrative (i.e., IRB office) review and approval of research studies qualifying for exempt or expedited review status

   When the IRB reviews research that involves subjects likely to be vulnerable to coercion or undue influence, policies and procedures dictate the IRB chair evaluate each protocol to ensure at least one IRB member is knowledgeable about or experienced in working with such subjects will be present at the meeting. The chair defers to another IRB or obtains consultation if there is not appropriate scientific or representational expertise.

b. Co-chair: Performs the responsibilities noted above [1.12 (a)] in the absence of the chair and/or as delegated by the chair

c. Administrator: Responsible for oversight of administration and operation of the IRB office; responsible for ensuring IRB and IRB office compliance with federal and state regulations and institutional policies governing human subject research and human subject research protections; assists in the provision and educational support to the research community

d. Regulatory Specialist: Responsible for ensuring compliance with federal regulations, and internal policies and procedures; oversees communication respective to federal-wide assurance agreements, inter-institutional

amendments and cooperative agreements, and is responsible for maintaining and updating IRB policies and procedures and IRB reference manual; provides education and support to research community, as well as to the IRB staff. Maintains up-to-date information regarding federal regulations and IRB policies related to the use of human subjects in research.

1.13 Definitions of Research and Human Subjects

(See Chapter 2, IRB Review of Research for more information on Designation of Research)

The Christ Hospital IRB is required to review and approve all research activity involving human subjects prior to implementation of research activity. A questions sometimes arises as to whether a planned activity is "research involving human subjects" and therefore requires IRB review and approval.

The Christ Hospital IRB Definition of Human Subjects Research: Under the organization's policies and procedures, an activity is human subjects research if it is either (1) human subject research subject to DHHS regulations, or (2) human subject research subject to FDA regulations.

DHHS Definition of Research and Human Subject

Research as defined by the DHHS regulations [45 CFR 46.102] shall mean a systematic investigation including research development, testing and evaluation designed to develop or to contribute to ***generalizable knowledge***. As defined in the Belmont Report, the term "research" designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (i.e., in theories, principles, and statements of relationships).

A ***human subject*** is defined by DHHS regulations [45 CFR 46.102(f)] as "a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information." ***Intervention*** includes both the physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. ***Interaction*** includes communication or interpersonal contact (e.g., questionnaires, interviews) between the investigator and the subject. ***Private information*** includes information about behaviors that occur in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by the individual and which that individual can reasonably expect will not be made public (i.e., a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may be readily ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

FDA Definition of Human Subject Research

Under FDA regulations [56.102] the term ***clinical investigation*** is synonymous with research and means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug and Cosmetic Act ("the Act") or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Act, but the results of which are intended to be later submitted to, or held for inspection by, The Food and Drug Administration as part of an application for a research or marketing permit. Clinical investigations regulated by the FDA under sections 505(i) and 520(g) of the Act includes investigations of food, dietary supplements that bear a nutrient content claim or health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. The term "clinical investigation" does not include experiments that must meet the provisions of Part 58 regarding non-clinical laboratory studies. The terms *research, clinical research, clinical study, study* and *clinical investigation* are deemed to be synonymous for purposes of this part. Research is subject to 21 CFR parts 50 and 56 when it involves the use of any drug other than the use of an approved drug in the course of medical practice. Research is subject to 21 CFR parts 50 and 56 when it involves the use of any medical device other than the use an approved medical device in the course of medical practice.

Human subject is defined under FDA regulations at 21 CFR 50.3(g) as "an individual who is or becomes a participant in research either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient." If the research involves a medical device, human subjects are individuals when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control [21 CFR 812.3(p)].

Test article defined by FDA means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

Subject defined by FDA means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or have a medical condition or disease [21 CFR 812.3(p)].

1.14 Innovative Practices vs. Research

Innovative or newly introduced procedures or therapies do not require IRB review and approval except when they include "research" as defined by the above criteria. An innovative clinical practice is an intervention designed solely to enhance the

well-being of the individual, patient or client. The purpose of the innovative clinical practice is to provide diagnosis, preventative treatment, or therapy to particular individuals. The introduction of innovative procedures or therapies into clinical practice (i.e., independent of a research activity approved by the IRB) should be reviewed with the applicable department chair and section chief, if applicable.

1.15 Quality Assurance vs. Research

Quality assurance projects do not require IRB review and approval except when the project involved includes "research" as defined by the above criteria. Precise definitions to permit the distinction between research studies and quality assurance projects are difficult and have not been established. In general, a quality assurance project is a project that is focused primarily on improving patient care within a given patient care environment (i.e., hospital or healthcare organization) and as such, the outcome of the project may not be generalizable to other patient care environments. Publication of a quality assurance project is not, per say, under the project "research"; however, if the outcome of a quality assurance project is published, attention should be given to avoiding the terminology "research" in the publication.

Questions directed at providing guidance and distinguishing quality assurance projects from research:

a. Is there a commitment in advance of data collection to a corrective plan given any one of several study outcomes? Does the principal investigator of the study have both clinical supervisory responsibility and the authority to impose change? If the answer to either question is no, then the study requires prior review and approval by the TCH IRB.
b. Is the research being sponsored/funded by an external agency? If yes, the study *may* require prior review and approval by TCH IRB.
c. Does the proposed study involve prospective assignment of patients to different procedures or therapies based on a predetermined plan such as randomization? If yes, the study requires prior review and approval by TCH IRB.
d. Does the proposed study involve a control group from which the therapeutic or study intervention is intentionally withheld to allow an assessment of its efficacy? If yes, the study requires prior review and approval by TCH IRB.
e. Will the study intervention be delivered in the blinded fashion, wherein neither the physician nor the patient knows to whom the study intervention or comparative intervention (i.e., placebo, standard care) was given? If yes, the study requires prior review and approval by TCH IRB.
f. Is the assessment of outcome blinded to the study intervention for the purpose of establishing efficacy of the intervention? If yes, the study requires prior review and approval by TCH IRB.

g. Does the proposed study involve the prospective evaluation of a drug, biologic or device that is not currently approved for general use by the FDA (i.e., to include evaluations of off-label indications)? If yes, the study requires prior review and approval by TCH IRB.
h. Will patients involved in a proposed study be exposed to additional risks or burdens (i.e., other than the completion of patient satisfaction surveys) beyond standard clinical practice in order to make the results of the study generalizable? If yes, the study requires prior review and approval by TCH IRB.

1.16 Research on or Involving Deceased Individuals

Research performed on individuals who have been declared legally dead and/or research involving the tissues of deceased individuals is not subject to review and approval of TCH IRB. (Note: Federal policy regulations governing human research subject protections define "human subjects" as living [emphasis added] individuals about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.) There are, however, ethical issues associated with research conducted on or involving deceased individuals. To address these issues, all personnel who desire to perform such research involving deceased individuals must submit a project application through their department chair. Research involving the medical records of the deceased individuals is subject to obtaining written consent of the descendant's next of kin or the executor of the descendant's estate. Please check with the HIPAA officer in the medical records department. For studies that include both living and deceased subjects, TCH IRB is the institutional community with jurisdiction for oversight and approval.