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PRINCIPAL INVESTIGATOR RESPONSIBILITIES

The principal investigator (PI) of a research study is ultimately responsible for the oversight and conduct of the research study including the informed consent process. They also maintain responsibility for assuring compliance with The Christ Hospital Institutional Review Board (TCH IRB) policies and procedures and any applicable regulations over their specific research project such as Department of Health and Human Services (DHHS) 45 CFR 46, and Food and Drug Administration (FDA) 21 CFR 50 regulations.

PI ASSURANCE AND RESPONSIBILITIES FORM

Principal Investigators must sign the PI Assurance and Responsibilities form which outlines their responsibilities with each study submission.

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE- CITI PROGRAM

The CITI Course will need to be completed every three years by any Principal Investigator and Sub-Investigator in active studies at The Christ Hospital. It is the policy of TCH IRB that investigators may not be listed as a Principal Investigator or sub-investigator unless proof of course completion is on file with the IRB Office.

See SOP 3.12 *Education of IRB Staff/Board Members/Investigators/Research Staff* for more guidance.

COMPLYING WITH IRB DECISIONS

In implementing research activities, the investigator is responsible for complying with IRB decisions, conditions, and requirements.

See SOP 2.04 *Complying with IRB Decisions* for more guidance.

REVIEW TYPES

Full Board

Under the full board review mechanism, the IRB may take one of four actions in regard to the protocol and informed consent:

Approved: The investigator is sent an approval letter, noting the date of expiration.

Approved with Modifications: Revisions and/or additional information specifically designated by the Institutional Review Board are sent to the investigator in an approval letter outlining the requested modifications. After making the designated revisions to the protocol and/or informed consent form, the investigator submits all requested changes

to the IRB Office with the revisions or additions underlined or highlighted with an accompanying cover letter referencing the TCH IRB number. Modifications that have been deemed minor by the IRB are applicable for expedited review and approval by the Chairman or designee, however, modifications that have been deemed major require full board review and approval. When the changes are reviewed and approved, an approval letter will be issued by the IRB Office and study activities may commence.

Tabled: If the Institutional Review Board requires major modifications and/or more information, then the protocol is tabled for a future convened meeting of the IRB. The investigator is sent a letter, which lists the reason(s) for deferral and includes a description of the revisions and/or clarifications requested. In some instances, one or more members of the IRB may be designated to discuss the reasons with the investigator. After revising the protocol and/or informed consent form, the investigator submits the revisions or additions underlined or highlighted with an accompanying cover letter referencing the TCH IRB number. The protocol is then rescheduled for review by the IRB at its next convened meeting. The investigator may be requested to present the protocol.

Disapproved: Disapproval of a protocol can occur when the IRB determines that the risk of the procedures outweigh any benefits that may be gained, or the study is not appropriate for The Christ Hospital. The investigator is sent a letter stating the reasons for disapproving the protocol.

See SOP 1.07 *Full Board Review Submission Guidelines* for more guidance.

Expedited

Under certain circumstances, the expedited review mechanism of The Christ Hospital Institutional Review Board may be invoked. Expedited Review is carried out by the IRB Chair or designee. All protocols approved by the expedited review mechanism are reported to the IRB at its next convened meeting (where quorum is present). The Chair or designee(s) will review the research evaluating whether the research fits the applicability, and if so, will determine whether the research fits into one or more of the categories for expedited review. The recommendations usually fall into three categories.

Approved: An approval letter is sent to the investigator following the expedited review.

Additional Information Requested: A letter or email is sent to the investigator, explaining what additional information is requested.

Full Board Review Required: The investigator is notified that full board review is necessary and the revisions and/or clarifications necessary are outlined for the submission of the protocol for review by the full board. The investigator submits the revised protocol to the IRB Chairman. The decision to require full board review is made if the protocol fails to meet the expedited review categories which are specified by federal regulations.

See SOP 1.17 *Expedited Review* for more guidance.

Exempt

Exemption designation review is conducted by the Chairman or designee. The reviewer may take one of three actions.

Exemption Approved: The investigator is sent an approval letter. A report upon completion of the study is required.

Additional Information Required: The investigator is sent a letter describing the information requested. The investigator submits a response to the IRB Chair for review. If the Chair or designee is satisfied that the protocol fulfills the exemption criteria, then the approval letter is sent to the investigator.

Exemption Disapproved: The investigator is sent a letter indicating that the new protocol does not fall within the exemption categories. A new application must be prepared and submitted for either expedited (if applicable) or full review by the IRB.

See SOP 1.07 1.16 *Exempt Research: Determination of Human Subject Research and Research Exempt from Federal Human Subjects Protection Regulations* for more guidance.

See Reference Sheet *Type of Review- Exempt, Expedited, and Full Board* for more guidance on the types of IRB review.

ASSURANCE OF COMPLIANCE

Some research projects involving human subjects require the submission of an Assurance of Compliance with HHS Regulations for the Protection of Human Research Subjects. Generally, these projects are those sponsored by the various federal agencies, i.e., NCI, NIH, and DHHS/FDA. The Christ Hospital maintains a FederalWide Assurance, FWA#00000702, on file with the Office for Human Research Protections (OHRP).

See SOP 1.02 *Federalwide Assurance* for more guidance.

DISCLOSURE OF FINANCIAL INTEREST

Each protocol submitted to the IRB for review must be accompanied by a Disclosure of Financial Interest Statement for each clinical investigator, sub-investigator, and all key research staff directly involved in the treatment or evaluation of research subjects in the study.

See SOP 2.13 *Investigator Disclosure of Financial Interest* for more guidance.

DISTRIBUTION AND RETENTION OF INFORMED CONSENT DOCUMENTS

The investigator is responsible for ensuring that each person signing an informed consent form is given a copy of the signed form, and one is filed in the medical record. Unless the research falls within the purview of the Food and Drug Administration (FDA), the investigator is responsible for retaining the signed consent and documents for at least three years after study closure or termination of IRB approval. For research that falls under FDA authority, the investigator is responsible for retaining the signed documents for the period specified in the applicable FDA regulations.

See SOP 2.02 *Informed Consent: Elements, Process and Documentation* for more guidance.

PROPOSED CHANGES/AMENDMENTS IN PREVIOUSLY APPROVED RESEARCH STUDIES

Significant changes or amendments to the protocol must be approved by the full board. Changes to the protocol cannot be initiated by the investigator without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject. An official request for approval on the change or amendment should be submitted to the IRB Chairman. The request should include the following: The TCH protocol number; the exact title of the protocol as originally submitted to the IRB; and a complete description of the nature of the changes. In addition, if the proposed changes necessitate a change in the consent form, then a revised consent form in which the revisions are tracked should be submitted.

Minor changes, amendments, or administrative modifications may be reviewed on an expedited review basis. Approval may be granted by the Chair or designee, unless the reviewer determines the nature of the proposed changes warrant a review by full board. The investigator is notified in writing of the IRB's decision.

A change in principal investigator or sub-investigators must be reported to the IRB. Also, if the research study is expected to extend beyond the time period initially approved by the IRB, then the investigator should submit a request for an extension of time to the IRB Chair.

See SOP 2.03 *Proposed Modifications/Amendments in Previously Approved Research Studies* for more guidance.

SUBMISSION OF IRB CERTIFICATION TO EXTERNAL FUNDING AGENCIES

After final IRB approval has been obtained, it is the investigator's responsibility to submit the proper certification to the sponsor/agency, if applicable. The IRB Office will provide necessary signatures when provided certification forms.

SUBMISSION OF CONTINUING REVIEW REPORTS

It is the principal investigator's responsibility to submit the required continuing review documentation or notification of study closure prior to expiration in the timeframe set forth in IRB Standard Operating Procedure 1.01- Continuing Review. According to federal and institutional regulations, the IRB must conduct continuing review of applicable approved human subject research protocols for purposes of renewal of the IRB approval period. For applicable research studies, typical review is annually, unless greater risk is identified by the IRB at the time of approval and more frequent reports are requested. However, review must occur within (1) one year from the date of approval per federal and institutional regulation. If continuing review and re-approval does not occur before the expiration date of IRB approval for an applicable studies, all research-related activity must cease unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Continuing review of applicable studies is required until Study Closure Report/Final Report form has been submitted to the IRB Office.

The investigator must submit the Continuing Review submission for review and approval at least six weeks prior to the expiration date to ensure time for studies requiring full board review. Submission documentation include:

- Continuing Review Report Form
- Current consent document for studies which remain active and enrolling subjects, or proposed consent document (if applicable)
- Any proposed amendments to the research (if applicable)
- Updated Disclosure of Financial Interest Form (if any new disclosures have occurred since last review)
- Protocol Deviation Log (IND, IDE, and HDE studies only), and
- CITI Transcripts for all key study personnel documenting the educational requirement has been completed within the last three years (for studies that remain active and enrolling subjects only).

At the time of review, if it is determined that additional information is necessary for consideration, or that irregularities have arisen which affect the participation of human subjects, the IRB may take the action to request revisions and/or additional information, request that the investigator attend the next IRB meeting, suspend IRB approval pending further investigation, or terminate IRB approval.

If the investigator fails to submit the Continuing Review Report by the submission deadline or fails to submit any requested information and the study does not get review and approval prior to the expiration date, the study expires automatically. all research-related activities must cease, including recruitment and enrollment of participants, interventions and interactions on current participants, collection of data and data analysis. There is no grace period extending the conduct of research beyond the expiration date of the IRB approval of the research. Extensions beyond the expiration date will NOT be granted. If stopping interventions or interactions will harm current participants, the investigator must submit a list of participants with a justification

of why they will be harmed by stopping the research procedures. The IRB Chair, in consultation with the Institutional Official, will determine which participants may continue in the research because of overriding ethical interest. The investigator will be provided a written determination. In the event of study expiration, the IRB Chair sends written notification regarding the study expiration to the Principal Investigator, Institutional Official, Appropriate Hospital Department Head, OHRP (for research covered by DHHS regulations), other federal agencies (for research is overseen by those agencies), and FDA (for FDA-regulated research).

See SOP 1.01 *Continuing Review* for more guidance.

PROTOCOL DEVIATION AND VIOLATION REPORTING

A protocol deviation and violation are very similar as both are any change, divergence, or departure from the approved study design or procedures of a research protocol that is under the investigator's control and that has not been approved by the IRB. However, a violation is a deviation that may affect the participant's safety, rights, or welfare and/or the completeness, accuracy, and integrity of the study data. The IRB requires the prompt reporting only of protocol violations within 10 business days to the IRB utilizing the Reportable Event form.

Investigators are required to obtain prior approval from the sponsor/clinical study manager before initiating major deviations (violations) from the investigational plan, except in emergency situations when it is necessary to protect life and/or well-being of a subject. Any such approval must be documented in writing and be maintained in the clinical study management and investigator files. Prior approval is not expected in situations where unforeseen events are beyond the investigator's control; however, such events are still deviations and should be reported on a protocol deviation log and/or kept in the study records.

Protocol deviations and violations should be documented in the study file, preferably on a log, to be reviewed at study specific intervals by the PI to determine if continuing noncompliance has occurred and becomes reportable. These logs are not required to be submitted to the IRB, unless for IND or IDE studies. The IRB requires the protocol deviation log for all IND and IDE studies to be submitted at the time of continuing review. The IRB Office may audit these files at any time.

See SOP 3.09 *Protocol Violation, Deviation, and Non-Compliance Reporting* for more guidance.

NON-COMPLIANCE REPORTING

The investigator must report any serious and/or continuing non-compliance to the IRB. Non-compliance is termed as the failure to comply with federal regulations, state laws, institutional policies, requirements or determinations of the IRB, and/or provisions of the approved research study. It is not considered noncompliance when there is a need to deviate from the approved protocol in order to protect the welfare of research participants. Serious non-compliance involves substantive potential or actual increased risk to the safety, rights and welfare of research

subjects. Continuing non-compliance involves repeated occurrences of noncompliance by the same investigator. Both serious and/or continuing noncompliance should be reported to the IRB within 10 business days utilizing the Reportable Event form.

See SOP 3.09 *Protocol Violation, Deviation, and Non-Compliance Reporting* for more guidance.

UNANTICIPATED PROBLEM (UAP) REPORTING

The Principal Investigator will promptly report unanticipated problems involving risks to subjects or others to the Institutional Review Board, in order to be investigated and action taken to protect subjects and others. Events involving risk to subjects or others must be reported as “Unanticipated Problems Involving Risks to Subjects or Others”. This category includes adverse events (medical occurrences) which meet the definition of an unanticipated problem (UAP) involving risk to subjects or others and other unanticipated problems that place subjects at risk of harm. The IRB will review and investigate the UAP to determine whether the event involves risks to subjects or others and, if so, what further action the situation necessitates.

An unanticipated problem is defined as any incident, experience, or outcome that meets all of the following three criteria:

- 1 Related or possibly related to the research if, in the opinion of the PI, it was more likely related to the research than not related to the research.
- 2 Unexpected because the nature, severity, or frequency of the event is not consistent with either the known foreseeable risks associated with the research that are described in the approved protocol, consent form, or other study-related documents (e.g., Investigator Brochure, product labeling, package insert)
or
Unexpected because the adverse event is not consistent with the expected natural progression of any underlying disease, disorder, or condition, of the subject(s) experiencing the adverse event and the subject(s) predisposing risks factor profile for the adverse event.
- 3 Suggests that the research places the subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

The IRB only requires the prompt reporting of unanticipated problems involving risks to participants and other within 10 business days to the IRB utilizing the Reportable Event form.

See SOP 2.05 *Reporting Unanticipated Problems (UAPs) Involving Risks to Subjects or Others* for more guidance.

NEWS RELEASES REGARDING RESEARCH

The Public Relations Department of The Christ Hospital has primary responsibility for the release of information to the news media or the public concerning human research projects. The IRB shall confirm the accuracy of all information regarding research protocols for use in press releases regarding research. When members of the news media contact physicians involved in such projects, calls must be referred to Public Relations. Any calls made to members of the news media must be made or cleared through Public Relations. Refer to The Christ Hospital Administrative Policy 4.30.110- *Release of Patient and Clinical Research Information to the News Media* for information on how calls should be handled.

See SOP 2.06 *News Releases or Recruitment Materials Regarding Research* for more guidance.

MATERIALS FOR RECRUITMENT OF SUBJECTS

All publications or media used to recruit subjects for research (i.e., radio, television, and newspaper advertisements) conducted at The Christ Hospital must be reviewed and approved by the IRB Chair.

See SOP 2.10 *Recruitment of Subjects in Research* for more guidance.

COMPLETION OF RESEARCH ACTIVITIES

The investigator must submit a final report and notify the IRB Chair when the research project is completed by submitting the Study Closure Report form. If the investigator fails to notify the IRB then he/she will continue to be responsible for completing the Continuing Review Reports. IRB protocol files will be maintained for a three-year period after study closure. At that time, the protocol file will be destroyed.

See SOP 2.07 *Notice of Study Closure* for more guidance.

HIPAA FULL AND PARTIAL WAIVER OF AUTHORIZATION

The HIPAA Privacy Rule establishes the conditions under which protected health information (PHI) may be used or disclosed by covered entities for research purposes, without specific patient authorization. In order to recruit individuals into research studies using PHI from The Christ Hospital, and contact the patient to seek informed consent and authorization for use and disclosure of PHI, the principal investigator must obtain partial waiver to Individual Authorization from the IRB by completing the *HIPAA Request for Partial Waiver to Individual Authorization* form. For retrospective chart reviews, the principal investigator must obtain a full waiver of authorization by completing the *HIPAA Request for Full Waiver of Authorization* form.

MINIMAL RISK, DEFINITION

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.