The Christ Hospital IRB
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IRB REFERENCE MANUAL
SECTION 03
CONTINUING IRB REVIEW OF EXISTING RESEARCH PROTOCOLS

3.0 CONTINUING IRB REVIEW OF EXISTING RESEARCH PROTOCOLS

3.1 Modifications to the Research Protocol and Informed Consent Document(s)

It is recognized that modifications of research protocols and informed consent documents may be required as the research study proceeds. *However, any proposed modification to an Institutional Review Board (IRB)-approved research protocol or informed consent document must be approved by the IRB prior to implementation.* The only exception to this requirement is a change in procedure that may be necessary to eliminate an apparent immediate hazard to a given research subject. It is not acceptable to modify extemporaneously (i.e., without prior IRB approval) an IRB-approved research protocol or consent form to permit the enrollment of a given individual who does not meet current eligibility criteria or to address any other specific issues related to the needs or desires of a given individual or patient who may want to participate in the study. Requests for protocol exceptions should be made in writing to the IRB Chair at the same time the request for exception is submitted to the sponsor.

3.1.1 Categories of Modification Review – Submission Requirements

IRB approval of modifications to research protocols and informed consent documents can be requested at any time. The approval of a modification request by the IRB will not, in general, alter the original IRB-approval date and expiration of IRB-approval dates assigned to the protocol. However, if the requested modification alters substantially the risk-to-benefit ratio of study participation, the The Christ Hospital (TCH) IRB may alter the expiration date assigned to the research protocol. The category of review (i.e., expedited or full board) of proposed modifications to an IRB-approved research protocol or consent document is dependent upon whether the proposed changes are considered minor or major. The IRB Chair or his/her designee shall have final responsibility for this designation.

3.1.1.1 Minor Modifications: The IRB Chair or his/her designee can expedite the review and approval of minor modifications to an IRB-approved research protocol or informed consent document. A minor modification is defined as a change that would not materially affect an assessment of the risks and benefits of the study or does not substantially change the specific aims or design of the study. Examples of minor modifications may include:

a. The addition of research activities listed under sections 2.2 Exempt Review or 2.3 Expedited Review
b. An increase or decrease in proposed human research subject enrollment (should be supported by a statistical justification)
c. Narrowing the range of inclusion criteria
d. Broadening the range of exclusion criteria
e. Alterations in the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration remain constant
f. Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations
g. An increase in the length of confinement or number of study visits for the purpose of increased safety monitoring
h. A decrease in the length of confinement or number of study visits, provided that such a decrease does not affect the collection of information related to safety evaluations
i. Alterations in human research subject payment or liberalization of the payment schedule with proper justification
j. Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement
k. The addition or deletion of qualified investigators and other key research personnel
l. The addition or deletion of study sites
m. Minor changes specifically requested by the IRB or Radiation Safety Committee

For minor modifications to a research protocol or informed consent document, submit the following:

n. The current research protocol with any modifications tracked
o. The current informed consent document with any modifications tracked
p. If applicable, a copy of the sponsor's research protocol amendment addressing the respective modification(s)

NOTE: Modifications to the informed consent document must take into account both prospective research subjects and, if applicable, research subjects already enrolled in the study. The latter may be addressed using an addendum to the initial informed consent document, or less preferably, by re-consenting the subject using the modified informed consent document.

3.1.1.2 Major Modifications: Major modifications to an IRB-approved research protocol or informed consent document must undergo full board review and approval. A major modification is defined as any change which materially affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study. Examples of major modifications may include:

a. Broadening the range of inclusion criteria
b. Narrowing the range of exclusion criteria
c. Alterations in the dosage or route of administration
d. Of an administered drug
e. Extending substantially the duration of exposure
f. The test material or intervention
g. Extending substantially the duration of exposure to the test material or intervention
h. The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations
i. The addition of serious, unexpected adverse events or other significant risks
j. Changes which, in the opinion of the IRB Chair or
his/her designee, do not meet the criteria or intent of a minor modification
k. Extending substantially the duration of exposure to the test material or intervention
l. The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations
m. The addition of serious, unexpected adverse events or other significant risks
n. Changes which, in the opinion of the IRB Chair or

his/her designee, do not meet the criteria or intent of a minor modification

For major modifications to a research protocol or informed consent document submit the following:

a. The current research protocol with any modifications tracked
b. The current informed consent document with any modifications tracked
c. If applicable, a copy of the sponsor's research protocol amendment addressing the respective modification(s)

NOTE: Modifications to the informed consent document must take into account both prospective research subjects and, if applicable, research subjects already enrolled in the study. The latter may be addressed using an addendum to the initial informed consent document, or less preferably by re-consenting the subject using the modified informed consent document.

3.1.2 Modification Turnaround Time

Minor modifications which qualify for expedited review will be reviewed by the IRB Chair or his/her designee in the order in which they were received in the IRB Office. Turnaround time varies depending upon the number of submissions received. Major modifications require full board review and investigators will receive correspondence from the IRB within approximately 5 working days of the scheduled meeting.

3.2 Research Protocol Renewals (Continuing Review and Status Updates)

The Christ Hospital IRB is responsible for continuing review of ongoing research to ensure that the rights, safety and wellbeing of human subjects are protected. However, due to changes associated with the 2018 Common Rule, certain applicable expedited studies approved on or after January 21, 2019 that are not subject to FDA-regulation, no longer require continuing review. While continuing review is no longer mandatory for these, TCH IRB does require the PI to submit an Annual Status Update for the study. Annual Status Updates are also required for research in which TCH relies on an external IRB (Reliance Agreements).

3.2.1 Review Period

3.2.1.1 Research in which TCH IRB (IRB of Record) provides oversight that <u>requires</u> continuing review:

At the time of initial review, The Christ Hospital IRB establishes a review period for each approved study that is appropriate to the degree of risk to subjects, but not less than once per year for applicable studies (see SOP 1.01 Continuing Review). For ease of tracking, the expiration date of applicable studies is set for the first day of the month of the year following the date that approval was granted (i.e., if approval is granted on June 14, 2022 the expiration date will fall on the June 1, 2023). The expiration date will be noted on the letter of approval and on subsequent continuing review approval letters. The expiration date is the first date that the protocol is no longer approved. TCH IRB also indicates in the letter of approval (on both initial and continuing review approval whether the study requires review more often than annually and whether the study requires verification from sources other than the investigator that no material changes have occurred since the previous TCH IRB review (21 CFR 56.108(a)(2)).

The Christ Hospital IRB requires that changes in approved IRB research activities be promptly reported to the IRB and that any changes in approved research, during the designated period of IRB approval, must not be initiated without IRB review and approval, except when the PI believes it necessary to eliminate apparent immediate hazard to the subject (21 CFR 56.108(b)(2) and 56.113).

The Christ Hospital IRB is authorized to suspend or terminate approval of research that is not being conducted in accordance with the TCH IRB requirements (21 CFR 56.108(b)(2) and 56.113).

3.2.1.2 Research in which TCH IRB (IRB of Record) provides oversight that <u>does not require</u> continuing review:

Research that presents no more than minimal risk to the participants and does not require full IRB Committee review is eligible for Expedited Review. Examples include blood draw within certain allowable volumes or non-invasive collection of biological specimens, such as a saliva swab. Changes associated with the 2018 Common Rule absolve certain applicable expedited studies, approved on or after January 21, 2019 that are not subject to FDA-regulation, of the requirement of continuing review. However, in certain circumstances, the IRB may determine it necessary to require continuing review of some research and will document the rationale for the decision to conduct continuing review using the expedited procedure.

When continuing review is not required, the IRB has implemented a brief "study status update" process to ascertain the status of each protocol that does not require formal continuing review to verify that no unapproved changes or unreported problems have occurred. The status check occurs annually. Researchers receive notification of an upcoming status check in advance of the annual period end-date. At the time of initial review, The Christ Hospital IRB sets an expiration date in the Mentor IRB system for one year following the date of approval for each approved study (see SOP 1.01 Continuing Review). For ease of tracking, this expiration date is set for the first day of the month of the following year that approval was granted (i.e., if approval is granted on June 14, 2022 the expiration date will fall on the June 1, 2023). The expiration date is noted as the "Next Check-In Date" on the letter of approval and on subsequent status update approval letters. A grace period may be given on a case-by-case basis for these research studies.

The Christ Hospital IRB requires that changes in approved IRB research activities be promptly reported to the IRB and that any changes in approved research, during the designated period of IRB approval, must not be initiated without IRB review and approval.

The Christ Hospital IRB is authorized to suspend or terminate approval of research that is not being conducted in accordance with these TCH IRB requirements.

3.2.2 Criteria for Approved Research

Federal and FDA regulations establish the criteria for TCH IRB approved research (45 CFR 46.111 and 21 CFR 56.111), as applicable. The criteria are the same for approval of continuing review and include the determination by TCH IRB that:

3.2.2.1 Risks to subjects are minimized

3.2.2.2 Risks to subjects are reasonable in relationship to anticipated benefits

3.2.2.3 Selection of subjects is equitable

3.2.2.4 Informed consent process is in place and appropriately documented

3.2.2.5 When appropriate, the research plan includes provision for monitoring of the data collected to ensure safety and

privacy of subject and confidentiality of the data

3.2.2.6 When appropriate, additional safeguards have been included to protect vulnerable subjects

3.2.3 Process for Continuing Review

3.2.3.1 PURPOSE: The purpose of continuing review is to review the progress of the entire study, not solely the modifications, for research in which TCH IRB serves as the IRB of record.

For FDA-regulated studies and all studies subject to the pre-2018 Common Rule Requirements continuing review may not be conducted through an expedited review process unless 1) the study was eligible for and initially reviewed by an expedited review procedure, or 2) the research is closed to enrollment of new subjects, and all subjects have completed all research related interventions, and collection and analysis of private identifiable information has been completed.

For research that is subject to the revised Common Rule, unless the IRB determines otherwise, continuing review is not required in the following circumstances:

a. Research eligible for expedited review in accordance with §46.110
b. Research reviewed by the IRB in accordance with the limited IRB review described in§46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8)
c. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
    - Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
    - Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

See SOP 1.01 Continuing Review, and 1.17 Expedited Review for more details.

3.2.3.2 FREQUENCY/EXTENT: The Christ Hospital IRB determines that the frequency and extent of continuing review for each study is adequate to ensure the continued protection of rights, welfare and privacy of research subjects. Factors under such consideration may include

the nature of the study, and the degree of risk involved and the vulnerability of the study population. The frequency and extent of continuing review are indicated in the approval letter and subsequent letters of approval of continuing reports.

3.2.3.3 DETERMINING CONTINUING REVIEW DATE: Federal regulations at 45 CFR 46.108(b) and 109(e) require respectively that (1) except when an expedited review procedure is used, each IRB must review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas; and (2) an IRB must conduct continuing review of research requiring review at intervals appropriate to the degree of risk, but not less frequently than once per year. The IRB should decide the frequency of continuing review for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects. For studies that meet criteria for a one-year review cycle, the IRB issues the expiration date for the first day of the month of the following year that approval was granted.

Several scenarios for determining the date of continuing review apply for protocols reviewed by the IRB at a convened meeting. To determine the date by which continuing review must occur, focus on the date of the convened meeting at which IRB approval occurs. (These examples presume the IRB has determined that it will conduct continuing review no sooner than within 1 year).

Scenario 1: The IRB reviews and approves a protocol without any conditions at a convened meeting on June 8, 2021. Continuing review must occur within 1 year of the date of the meeting, that is, by June 1, 2022.

Scenario 2: The IRB reviews a protocol at a convened meeting on June 8, 2021 and approves the protocol contingent on specific minor conditions the IRB Chair or his/her designee can verify. On July 15, 2021 the IRB Chair or designee confirms that the required minor changes were made. Continuing review must occur within 1 year of the date of the convened IRB meeting at which the IRB reviewed and approved the protocol, that is, by June 1, 2022.

Scenario 3: The IRB reviews a study at a convened meeting on June 8, 2021 and has serious concerns, or lacks significant information, that required subsequent IRB

review of the study at the convened meeting on July 13, 2021. At their July 13, 2021 meeting, the IRB completes its review and approves the study. Continuing review must occur within 1 year of the date of the convened meeting at which the IRB reviewed and approved the protocol, that is, by July 1, 2022.

3.2.3.4 PI RESPONSIBILITY: The PI is responsible for the prompt reporting to the IRB. This includes continuing review reports by the stated date in the approval letter. Mentor IRB will send a courtesy reminder 4 weeks before the submission deadline date. A continuing review submission must be submitted into Mentor IRB by the due date indicated (three weeks prior to the convened IRB meeting scheduled immediately preceding the approval expiration date) to allow adequate IRB review at the next regularly scheduled meeting. This form must be submitted until a study closure request has been submitted into Mentor IRB (see SOP 2.07 Study Closure). Mentor IRB sends notifications to the PI and research coordinators if the submission has not been submitted by the due date. The IRB Office also will follow-up with a phone call and/or email message.

Scenario: A study has an expiration date of 10/01/2022. This study must be reviewed by the full board at the September 13 convened IRB meeting. The deadline for submission of the report to the IRB is 3 weeks prior to the meeting date, August 23, 2022.

3.2.3.5 STUDY EXPIRATION: The continuation of research after expiration of IRB approval is a violation of federal and FDA regulations. If TCH IRB has not received, reviewed and approved a research study by the study's current expiration date, i.e., TCH IRB approval has expired, research activities must cease. A study expiration letter is generated through Mentor IRB and will be sent to the PI and any research coordinators. No new subjects may be enrolled. If the PI is actively pursuing renewal with the TCH IRB and the IRB determines that an overriding safety concern or other ethical issue is involved, the IRB may permit the study to continue for the brief time required to complete the review process. All currently participating subjects should be notified that the study has been terminated. Procedures for withdrawal of enrolled subjects should consider the rights and welfare of the subjects. If follow up of subjects for safety/welfare reasons is permitted/required by the IRB, the subjects should be

notified, and adverse events and outcomes should be reported to the IRB and sponsor.

3.2.3.6 EXPEDITED REVIEW: TCH IRB uses the expedited review procedure to review (1) some or all research studies appearing on the list [RM 2.3] and found by the reviewer to involve no more than minimal risk; (2) minor changes in previously approved research during the period (of one year or less) for which approval is authorized, done by the Chair or by an experienced person delegated by the Chair to review from TCH IRB. In this process the reviewer may exercise all the authorities of the IRB except to disapprove the research. A research activity may be disapproved and only after review in accordance with non-expedited review set forth in 21 CFR 56.108(c). The reviewer will present the expedited review report at the next full board meeting for consideration, discussion and acknowledgment.

3.2.3.7 FULL BOARD REVIEW: Each continuing review report (non-expedited) will be presented to the full board for consideration, discussion and vote for approval, modification for approval or disapproval. Appropriate correspondence will be forwarded to the PI in a timely fashion with a letter for a) approval with date for next review; b) approval pending modification with date for next review; or c) disapproval and notice of termination of the study.

3.2.4 Process for Status Updates

3.2.4.1 PURPOSE: Annual study status updates serve multiple functions. They ensure the institution is aware of all research that is currently ongoing within the institution. It also allows a mechanism for annual study specific FCOI disclosures and review of investigator and research personnel training requirements (i.e. CITI HSR and GCP training). Annual Status Updates are submitted via the Mentor IRB system and have been designed to collect a very limited amount of information from the study team. The completed annual status report must be received by the due date. If the researcher does not submit an Annual Status Update, the IRB may consider this noncompliance. The status update is reviewed and approved through the expedited mechanism by the IRB Chair or experienced person delegated by the Chair to review from TCH IRB. See SOP 1.01 – Continuing Review and 1.17 – Expedited Review for more details.

3.2.4.2 FREQUENCY/EXTENT: Status Updates occur annually. The Next Check-In Date is indicated in the approval letter. The Next Check-in Date serves as the expiration date in Mentor IRB.

3.2.4.3 DETERMINING NEXT CHECK-IN DATE: The IRB issues the Next Check-In Date for the first day of the month of the following year that approval was granted. The due date for submission is four weeks prior to the Next Check-In Date.

Example: The IRB Chair or designee reviews and approves the status update on June 8, 2022. The next study status update Check-In Date is June 1, 2023. The due date for the status update is May 1, 2023.

3.2.4.4 PI RESPONSIBILITY: The PI is responsible for the prompt reporting to the IRB. This includes status updates by the stated date in the approval letter. Mentor IRB will send a courtesy reminder 2 weeks before the due date. A status update submission must be submitted into Mentor IRB by the due date indicated to allow adequate time for review. Status updates must be submitted annually until a study closure request has been submitted into Mentor IRB (see SOP 2.07 Study Closure). Mentor IRB sends notifications to the PI and research coordinators if the submission has not been submitted by the due date. The IRB Office also will follow-up with a phone call and/or email message.

3.2.4.5 STUDY EXPIRATION: If TCH IRB has not received, reviewed and approved a research study by the study's current expiration date in Mentor IRB, the IRB is authorized to suspend or terminate the research. A notice of study expiration will be sent to the PI and any research coordinators through Mentor IRB. The IRB may extend a grace period on a case-by-case basis.

3.2.5 Continuing Review Report

A Continuation Form must be completed in its entirety in Mentor IRB and submitted for consideration along with a copy of the most recently approved consent form(s) and study specific FCOI Disclosures for all investigators and key research staff.

3.3 Reporting Unanticipated Problems Involving Risks to Human Subjects

Federal and FDA regulations at 45 CFR 46.108(a)(4)(i) and 21 CFR 56.108(b)(1) require IRBs to have written procedures for ensuring prompt

reporting to the IRB of any unanticipated problems involving risks to subjects or others. Consistent with these regulations and IRB policies, investigators are required to report unanticipated problems involving risks to human subjects or others following the procedures outlined in Section 8.0 "Reporting Unanticipated Problems Involving Risks to Human Subjects/Adverse Events". See SOP 2.05- Reporting Unanticipated Problems (UAPs) Involving Risks to Subjects or Others for reporting requirements.

3.4 Reporting Protocol Deviations/Violations

A protocol deviation occurs when there is a 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, and does not affect the participant's safety, rights, or welfare and/or the completeness, accuracy and integrity of the study data. A protocol violation is any deviation that does affect the subject's rights, safety, or welfare, and/or the completeness, accuracy and integrity of the study data. The term "violation," though sometimes used interchangeably with "deviation," is often considered a major, more serious, variance from an approved protocol than a deviation. Protocol deviations do not require IRB reporting, yet should be documented in the study file to be reviewed at specific intervals by the PI to determine if it constitutes continuing non-compliance and becomes reportable. Protocol violations must be reported to the IRB on the Reportable Event Form. See SOP 3.09- Protocol Violation, Deviation, and Non-Compliance Reporting for more details.

3.5 Revised Sponsor Protocols or Investigator Brochures

Revised sponsor protocols or investigator brochures must be submitted to the IRB in a timely manner. The submission of a revised sponsor protocol or investigator brochure should include a memo from the principal investigator indicating his/her review of the document as well as an assessment of whether changes are required to the approved IRB protocol and/or consent document.

3.6 Research Protocol Suspension or Termination

3.6.1 Definitions

IRB-Initiated suspension of approval: IRB-initiated suspension of approval refers to a determination made by TCH IRB to temporarily withdraw IRB approval for some or all activities of a currently approved research study.

IRB-Initiated termination of approval: IRB-initiated termination of approval refers to a determination made by TCH IRB to permanently withdraw IRB approval for some or all activities of a currently approved research study.

Investigator-initiated suspension of approval: Investigator-initiated suspension of approval refers to a determination made by the principal investigator or sponsor of the research study to temporarily suspend some or all activities of a currently approved research study.

Investigator-initiated termination of approval: Investigator-initiated termination of approval refers to a determination made by the principal investigator or sponsor of the research study to permanently terminate some or all activities of a currently approved research study.

Serious non-compliance: Failure to comply with any of the federal or state regulations or institutional policies governing human subjects research that, in the judgment of TCH IRB, seriously compromises human research subjects protection or the integrity of TCH IRB's human research protection program. Examples of serious non-compliance include, but are not limited to:

3.6.1.1 Performing non-exempt human subject research without obtaining TCH IRB approval

3.6.1.2 Failing to obtain TCH IRB approval of substantial modifications implemented in a TCH IRB-approved research study

3.6.1.3 Failing to systematically obtain the required written or, when prior-approved by TCH IRB, verbal informed consent of research subjects

3.6.1.4 Material failure of TCH IRB (including TCH IRB Office staff) to comply with federal regulations governing human subject protections

3.6.2 IRB-Initiated Suspension or Termination of a Research Protocol

The IRB has the authority to suspend or terminate its approval of a research protocol that is not being conducted in accordance with regulatory or IRB requirements or that is associated with serious harm to human research subjects. Such suspension or termination of approval shall be reported promptly to the investigator and shall include a written statement of the reasons for the IRB's action. Suspension or termination of IRB approval initiated by the IRB shall be reported to the Authorized Institutional Office and, if applicable, to the Office of Human Research Protections (for federally funded research), the FDA (for research subject to FDA oversight), the sponsor (e.g., industry sponsor or federal granting agency), and/or

other relevant regulatory agencies.

3.6.3 Investigator/Sponsor-initiated Suspension or Termination of a Research Protocol – IRB Notification

3.6.3.1 Suspension or termination of an IRB-approved research protocol by the principal investigator and/or sponsor of the research study shall be reported promptly (i.e., within 1 day of receipt of the sponsor suspension/termination notice) to the IRB Office and in Mentor IRB if the suspension/termination is based on a change in the risk-to-benefit ratio of study participation (e.g., serious adverse events, non-effectiveness of the research intervention). Suspension/termination of a research study for other (e.g., administrative) reasons shall be reported in Mentor IRB within 10 working days of receipt of the suspension/termination notice. IRB notification shall include:

a. The reason for study suspension or termination (e.g., subject accrual complete and data analyzed; demonstrated absence of benefit based on interim data analysis; serious adverse event)
b. The number of subjects currently enrolled in the study at The Christ Hospital and the status (e.g., currently undergoing research intervention and monitoring; completed intervention follow-up monitoring only; completed study) of each enrolled subject
c. A description of the procedures that will be used to notify subjects currently participating in the study of the study suspension/termination; the procedures that will be undertaken to ensure their orderly and safe withdrawal from the study; follow-up care, if applicable
d. A description of the procedures that will be used to notify subjects who previously participated in the study of the study suspension/termination, if determined to be important to their rights or welfare.

3.6.3.2 For terminated research protocols, a study closure should be requested in Mentor IRB within 10 working days of notification of closure by the sponsor. This request will be reviewed and acknowledged by IRB Chair or Designee. The acknowledgment will be documented in the protocol record and assigned to the Expedited/Exempt Report for review, consideration, discussion and acknowledgment by

the convened IRB. The PI and any research coordinators will receive an acknowledgment notification through Mentor IRB after chair review.

Study Closure is defined by TCH IRB as *all* of the following having been accomplished: 1) all subjects have completed final visits and follow up, 2) the sponsor or its representative has indicated closure at the research site, 3) if the study was conducted under a Federal Wide Assurance, all data analysis at the site is completed.

3.6.3.3 For research protocols suspended due to serious adverse events, IRB approval is required to reinitiate the research study. The written request for study re-initiation shall address:

a. The outcome of investigations on the causality of the serious adverse event(s)
b. The frequency of occurrence of the serious adverse event(s) at TCH IRB or external sites, if applicable
c. Modification of the protocol and consent form to address the serious adverse event(s)

3.6.4 Research Protocol Suspension or Termination - Human Research Subject Notification and Withdrawal

Human subjects currently participating in a research study must be notified of its suspension or termination due to safety issues and/or other problems (e.g., unanticipated problems, failure to obtain continuing IRB approval, investigator non-compliance) and the reasons, therefore. It is strongly recommended that such notification be in the form of a consent form addendum to document subject receipt and understanding of this information. Procedures for withdrawal of enrolled human research subjects should consider their rights and welfare. If follow-up of the subjects for safety or effectiveness reasons is permitted or required by the IRB (e.g., under a research protocol that is suspended or closed to enrollment), the subjects should be so informed (i.e., through the use of a consent form addendum) and any adverse events or other outcomes identified during follow-up should be reported to the IRB, the research study sponsor, authorized institutional official, OHRP and the FDA, if applicable.

3.6.5 IRB Record Retention Following Study Termination

Research files will be retained by the IRB Office for three years after completion of the research (45 CFR 46.115(b) and/or 21 CFR 56.115(b)).

3.7 Study Audits

The IRB conducts audits of research studies annually. A minimum of two audits will be performed yearly. See SOP 1.09- Quality Improvement Activities in Human Research Protection/Audits.

3.7.1 Selection of Studies to Review

Research studies will be chosen for Quality Assurance (QA)/Quality Improvement (QI) review primarily from among studies meeting one or all the following characteristics:

3.7.1.1 Does not receive study monitoring by the study sponsor or another organization

3.7.1.2 Presents greater than minimal risk to participants

3.7.1.3 Involves investigator-initiated research

3.7.1.4 Enrolls vulnerable populations, including TCH employees and students, cognitively impaired participants, pregnant women/fetuses/neonates and children

3.7.1.5 Has potential for conflict of interest

3.7.1.6 Are requested by the IRB or institutional official