The Christ Hospital IRB
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STANDARD OPERATING PROCEDURE

Proposed Amendments/Modifications in Previously Approved Research Studies

1.0 POLICY

An amendment, or modification, to an IRB-approved research study is a proposed change in the conduct of the study, including (but not limited to) any change, revision, or addition to an approved study protocol, informed consent, or related document(s), that may affect the protection of human subjects.

Any amendment or modification may not be implemented until IRB approval is granted. The only exception is when a change is necessary to eliminate apparent immediate hazards to the research subjects. Such unanticipated risks to subjects, or new information that may affect the risk-benefit assessment, must be promptly reported to and reviewed by the IRB to ensure adequate protection of human subjects.

Minor amendments or modifications may be reviewed in an expedited procedure by the IRB chair or authorized designee in accordance with 45 CFR 46.110 and 21 CFR 56.110. However, significant amendments or modifications must be approved by the Full Board at a convened meeting. Refer to Section 03 of the IRB Reference Manual, "Modifications to and Continuing IRB Oversight of Existing Research", for additional information on amendments and modifications.

2.0 OVERVIEW

2.1 Minor Amendments/Modifications

Minor amendments or modifications to an IRB-approved research protocol may be reviewed on an Expedited Review basis. Approval may be granted by the IRB chairman and/or a designated representative, unless the reviewer(s) determines that the nature of the proposed changes warrants a review by the Full Board. In that instance, the investigator shall be informed in writing that the review requires Full Board review and will subsequently be notified in writing of the Board's decision. Examples of minor modifications may include:

2.1.1 Changes (addition or removal) of investigators or research staff engaged in human subjects research, such as:

2.1.1.1 Addition of Personnel: To be considered for addition to a study, proposed key research personnel must:

2.1.1.1.1 Remain current in CITI training (completed within the most recent three years) in Human Subject Research (HSR) and Good Clinical Practice (GCP), as applicable (ref. IRB SOP 3.12 - Education of IRB Staff/Board Members/Investigators/Research Staff):

2.1.1.1.2 Complete institutional training in Financial Conflict of Interest (FCOI) Disclosures in Research:

2.1.1.1.3 Remain current in FCOI training (completed within the most recent three years), included in the CITI HSR training course, after the initial institutional FCOI training:

2.1.1.1.4 Complete an Annual FCOI disclosure (ref. IRB SOP 2.13 "Investigator and Other Key Research Personnel Disclosure of Financial Interest").

2.1.1.2 Removal of Personnel:

2.1.2 The addition of research activities to exempt or minimal risk research

2.1.3 An increase or decrease in proposed human research subject enrollment, supported by a statistical justification

2.1.4 Narrowing the range of inclusion criteria

2.1.5 Broadening the range of exclusion criteria

2.1.6 Decreasing the number or volume of biological sample collections, provided that such the change does not affect the collection of information related to safety evaluations

2.1.7 An increase in the length of confinement or number of study visits for the purpose of increased safety monitoring

2.1.8 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

2.1.9 Alterations in payment to human research participants or liberalization of the payment schedule with proper justification

2.1.10 Changes to improve the clarity of statements or to correct typographical errors in approved study materials, provided that such a change does not alter the content or intent of the statement

2.1.11 The addition or deletion of study sites

2.1.12 Minor changes specifically requested by the IRB

2.1.13 Requests to extend the study beyond the period of time initially approved by the IRB

2.2 Major modifications

Major modifications to an IRB-approved research protocol 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:

2.2.1 Broadening the range of inclusion criteria
2.2.2 Narrowing the range of exclusion criteria
2.2.3 Alterations in the dosage or route of administration of an administered drug;
2.2.4 Substantially extending the duration of exposure of the test material or intervention
2.2.5 The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations
2.2.6 The addition of serious, unexpected adverse events or other significant risks
2.2.7 Changes which, in the opinion of the IRB chair or his/her designee, do not meet the criteria or intent of a minor modification

NOTE: Revisions to the informed consent document must account for both prospective research participants and, if applicable, research participants already enrolled in the study. The latter may be addressed by using an addendum to the initial informed consent document, or by re-consenting the research participant using the revised informed consent document.

3.0 PROCEDURE

3.1 Principal Investigator

3.1.1 Submits the proposed amendment or modification in Mentor IRB. The request should include the following, as applicable to the amendment:
- 3.1.1.1 Complete description of the nature of the changes
- 3.1.1.2 Clean and tracked-changes copies of the amended research protocol
- 3.1.1.3 The sponsor's summary of changes document addressing the respective modification(s)
- 3.1.1.4 Clean and tracked-changes copies of the revised consent form(s)
- 3.1.1.5 New study materials
- 3.1.1.6 Clean and tracked changes copies of revised study material(s)

3.1.2 Presents the amendment at the convened IRB meeting, if requested
3.1.3 Awaits notification of IRB approval prior to implementing any changes.

3.2 IRB Chair or Board

3.2.1 **Minor Amendments/Modifications**
The IRB chair reviews the modification utilizing the "Chair Expedited Review – Amendment" Reviewer Checklist in Mentor IRB and makes one of the following determinations:

3.2.1.1 Approved
3.2.1.2 Approved with modifications
3.2.1.3 Referred to Full Board for review

3.2.2 **Major (Significant) Amendments/Modifications**

3.2.2.1 The IRB Chair and/or other designated reviewer reviews the submission utilizing the "Primary Reviewer – Amendment" Reviewer Checklist in Mentor IRB.
3.2.2.2 The IRB Chair and/or other designated reviewers lead the discussion at the convened meeting
3.2.2.3 The convened IRB reviews the submission and makes its determination at a convened IRB meeting with quorum present.

3.3 IRB OFFICE STAFF

3.3.1 **Minor Amendments/Modifications**

The IRB office staff:

3.3.1.1 Ensures that the submission is complete and assigns the reviewer checklist to the IRB chair/authorized designee for review in Mentor IRB
3.3.1.2 Consults the IRB chair/authorized designee in making the initial review type determination, as necessary
3.3.1.3 Sends correspondence to the Principal Investigator as directed by the IRB chair/authorized designee, indicating the determination
3.3.1.4 Assigns the amendment to the Exempt/Expedited Report Panel to be included in the Exempt/Expedited Report (Chairman's Report) for the awareness of the convened board at the next scheduled meeting

3.3.2 **Major Amendments/Modifications**

The IRB office staff:

3.3.2.1 Ensures that the submission is complete and available in its entirety in Mentor IRB for IRB member review approximately two weeks prior to the convened meeting date;
3.3.2.2 Assigns the amendment to the Full Board Panel which places the protocol on the next convened IRB's meeting agenda for review;
3.3.2.3 Assigns the "Primary Reviewer – Amendment" checklist to the IRB chair/authorized designee for review in Mentor IRB for completion prior to the convened meeting
3.3.2.4 Records discussion and determinations on modifications in the meeting minutes
3.3.2.5 Following the IRB Chair's initial approval of the meeting minutes, communicates all IRB determinations (through Mentor IRB) in a notification letter sent to the principal investigator and any research coordinator(s) as outlined in SOP 1.04 - Conducting

4.0 REFERENCES

4.1 IRB Standard Operating Procedures
- 4.1.1 SOP 3.12 - Education of IRB Staff/Board Members / Investigators / Research Staff
- 4.1.2 SOP 2.13 - Investigator and Other Key Research Personnel Disclosure of Financial Interest
- 4.1.3 SOP 1.04 - IRB Meeting Minutes / Conducting IRB Meeting

4.2 IRB Reference Manual: Section 3.0 of the IRB Reference Manual

4.3 IRB Electronic Record Management System: Mentor IRB

4.4 Code of Federal Regulations
- 4.4.1 U.S. Department of Health and Human Services (HHS) 45 CFR 46.110
- 4.4.2 U.S. Food and Drug Administration (FDA) 21 CFR 56.110

4.5 AAHRPP Domains and Elements
- 4.5.1 II.2.E.3
- 4.5.2 II.2.F.3