The Christ Hospital IRB
Submitted By: Erica Jones, CIP
Approved By: Steve Roberts, MD

Number: 2.02
Effective Date: 01/09
Revision Date: 05/26

STANDARD OPERATING PROCEDURE

Informed Consent: Elements, Process, and Documentation

1.0 POLICY

It is The Christ Hospital's policy that research may not include human subjects without the informed consent of the research participant or his/her Legally Authorized Representative (LAR), unless a recognized exception or waiver applies under federal regulations (ref. IRB SOP 3.15, Waiver, Alterations, and Exceptions to Informed Consent). An investigator shall seek informed consent in accordance with federal regulations at 45 CFR 46.116 and, if applicable, 21 CFR 50.20, 21 CFR 50.25, and any applicable regulations of the sponsor, unless the IRB grants a waiver of informed consent in accordance with 45 CFR 46.116(f)(1), 45 CFR 46.116(d), and (if applicable) 21 CFR 50.23(d) and (e), 21 CFR 50.24, and the U.S. Department of Health and Human Services (HHS) Waiver of Informed Consent Requirements in Certain Emergency Research at 61 FR 51531, or any applicable regulations of the sponsor. Additionally, an investigator will document informed consent in accordance with 45 CFR 46.117 and, if applicable, 21 CFR 50.27, or other applicable regulations of the sponsor unless the IRB waives documentation of informed consent in accordance with 45 CFR 46.117(c)(1), and, if applicable, 21 CFR 56.109(c), 21 CFR 56.109(d) or other regulations of the sponsor. The principal investigator is responsible for ensuring that informed consent is obtained from each research participant before the individual participates in a research study. Although the principal investigator may delegate duties for obtaining informed consent to other members of the research team, he/she remains ultimately responsible for the informed consent process.

If consent or documentation of consent has not been waived by the IRB, in order to approve research the IRB will determine that informed consent will be (1) sought from each prospective research participant or his/her Legally Authorized Representative and (2) appropriately documented in accordance with and to the extent required by federal regulations at 45 CFR 46.111, 45 CFR 46.116 and 45 CFR 46.117, and 21 CFR 50.20, 21 CFR 50.25, 21 CFR 50.27 and 21 CFR 56.111, if applicable, and any applicable regulations of the sponsoring agency. The IRB will determine whether additional information required by federal regulations should be included in the informed consent process in accordance with 45 CFR 46.109(b), and whether any other disclosures should be included in the informed consent process as required by other federal, state, or local laws or regulations to make the informed consent process legally effective. All IRB determinations under this policy will be made at the time of initial review, continuing review, and review of modifications to research.

1.1 Additional Safeguards for Vulnerable Groups

In addition to the other responsibilities described in this policy, the IRB and investigators will employ additional safeguards to preserve the informed consent process when some or all participants are likely to be vulnerable to coercion or undue influence. At the time of initial review, continuing review, and review of modifications to research, the IRB will systematically evaluate whether the research involves participants likely to be vulnerable to coercion or undue influence and will consider appropriate additional safeguards for the informed consent process. Research will incorporate safeguards for pregnant women, fetuses, and neonates in accordance with 45 CFR Part 46, Subpart B and, if applicable, any applicable regulations of sponsoring agencies. Note: The Christ Hospital does not engage in research on prisoners.

Where federal regulations or guidance exist to provide standards for safeguards to preserve the informed consent process for participants vulnerable to coercion or undue influence, such safeguards will conform to specific institutional policy and procedure or, when no institutional policy and procedure exists, written procedures developed by the IRB. IRB procedures developed for the informed consent process utilized with vulnerable groups will take into account:

1.1.1 The decision-making capacity of the participants;
1.1.2 Likely circumstances producing coercion or undue influence;
1.1.3 The magnitude of the effect on participants' ability to knowingly and voluntarily consent;
1.1.4 Appropriate options to neutralize coercive or undue effects; and
1.1.5 If participants are unable to give legally effective consent, adequate provisions are made for soliciting the assent of the participants and the permission of their legally authorized representatives.

(Ref. SOP 3.18 Additional Safeguards for Individuals Without Decision-making Capacity)

The IRB or IRB chair may authorize an IRB staff member, or a disinterested third party, to observe the informed consent process. This may typically be requested if the study is determined to have more than minimal risk involved, or if the study has the potential to enroll vulnerable populations. Observation of the consent process may only be performed with the consent of the research participant. Ref. 45 CFR 46.109(e); 21 CFR 56.109(f)

1.2 Illiterate English-Speaking Subjects

A person who speaks and understands English but does not read and write may be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law. A person who can understand and comprehend spoken English, but is physically unable to speak or write, may be entered into a study if they are competent and able to indicate approval or disapproval by other means. If the person (1) retains the ability to understand the concepts, risks and

benefits of being in the study when it is explained verbally (still competent), and (2) can indicate approval or disapproval to study entry, they may be entered into the study. The consent form should document the method used for communication with the prospective research participant and the specific means by which the prospective participant communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document.

2.0 PROCEDURE

2.1 Investigator Responsibilities

2.1.1 Initial IRB Submission

At the time of initial IRB submission, the investigator shall:

2.1.1.1 Submit the e-application having completed the appropriate sections describing the consent process including:

2.1.1.1.1 Identification of the individuals authorized to conduct informed consent discussions with prospective research participants;

2.1.1.1.2 When and where informed consent may be obtained;

2.1.1.1.3 How it will be determined that the subject understands the information provided;

2.1.1.1.4 How consent will be handled when a subject's decision-making capacity is in question;

2.1.1.1.5 Any additional safeguards added to the informed consent process to protect vulnerable populations from undue influence and coercion, if applicable;

2.1.1.1.6 Any request of a waiver or alteration of informed consent requirements, including documentation, when appropriate (ref. IRB SOP 3.15 Waiver, Alterations, and Exceptions to Informed Consent)

2.1.1.1.7 Identifying and requesting exceptions to the informed consent process, as appropriate, for clinical investigation subject to the Food and Drug Administration (FDA) regulation (ref. IRB SOP 1.10 Emergency Use Of An Investigational Drug, Biological Product, or Device);

2.1.1.1.8 Any information to be disclosed to participants which meets the requirements for the informed consent process that is NOT exhibited in the proposed informed consent documents; and

2.1.1.1.9 Any request for approval for the use of a Legally Authorized Representative to consent on a subject's behalf, if appropriate, for the subject population. Note: IRB approval is required for the use of Legally Authorized Representatives.

2.1.1.1.10 How much time will be given to potential subjects to consider participation in the research. Note: Adequate time should be provided for the potential participant to read the informed consent document and consider the risks and benefits prior to signing. If consent is obtained the same day that the participant's involvement in the study begins, the participant's medical record/case report form should document that consent was obtained prior to participation in the research.

2.1.1.2 Submit the proposed informed consent document(s) including, but not limited to, the following requirements for the informed consent process (unless a waiver or exception of informed consent process is requested). Ref. IRB Informed Consent Template:

2.1.1.2.1 Basic elements of consent in accordance with federal regulations at 45 CFR 46.116(a) and, if applicable, 21 CFR 50.20;

2.1.1.2.2 Additional elements of consent, when appropriate, in accordance with federal regulations at 45 CFR 116(c);

2.1.1.2.3 Use of simple language at the appropriate reading and comprehension level, or that is appropriate to the specific subject population (approximately 6th grade reading level for adult consent documents); and

2.1.1.2.4 Avoidance of complicated or medical/technical language, replacing such language with lay terms to ease subject comprehension.

2.1.2 **Consent**

At the time of consent, the investigator shall:

2.1.2.1 Verify, when applicable, that a LAR meets the order of priority for granting permission for participation of the proposed research participant;

2.1.2.2 Obtain signatures and dates of signatures on the informed consent document for the following individuals, unless the IRB has waived documentation of informed consent process:

2.1.2.2.1 Participant or LAR, if applicable;

2.1.2.2.2 Witness/person obtaining informed consent: In the case of illiterate subjects, an impartial third party should witness the entire consent process and also sign the consent document;

2.1.2.2.3 Provide a copy of the signed IRB-approved informed consent document to the individual who signed the form (participant or LAR, as applicable), unless waived by the IRB;

2.1.2.2.4 Supply a copy of the signed informed consent document to performance sites in accordance with the performance site's policy;

2.1.2.2.5 Keep the original signed consent form in the subject's research file;

2.1.2.2.6 Retain the signed consent and documents for at least three years after termination of IRB approval and closure of the protocol, unless the research falls within the purview of the FDA;

2.1.2.2.7 Retain the signed documents for the period specified in the applicable FDA regulations for research that falls under FDA authority; and

2.1.2.2.8 Submit any revisions to the informed consent process or documents to the IRB for review and approval using the amendment/modification procedure (ref. SOP 2.03 Proposed Modifications/Amendments in Previously Approved Research Studies).

2.2 IRB Chair Responsibilities

2.2.1 Initial Review of Consent Processes

At the time of Initial Review, the IRB chair shall:

2.2.1.1 Review submissions to assess whether sufficient information on the proposed informed consent process and documentation for informed consent has been provided for convened IRB review, and request additional information if necessary;

2.2.1.2 Examine submissions for requests for waiver of informed consent, waiver of consent documentation, or HIPAA partial waiver requests (ref. TCH IRB SOP 3.15 Waiver, Alterations, and Exceptions to Informed Consent);

2.2.1.3 Review all informed consent documents submitted for IRB review for required and additional elements, as appropriate; and

2.2.1.4 Request additional information, as needed, to the protocol or informed consent documents and correspond with the investigator requesting such information.

2.2.2 Initial Expedited Review of Consent Processes

At the time of Initial Expedited Review, the IRB chair shall:

2.2.2.1 Review submissions to assess whether sufficient information is provided on the proposal;

2.2.2.2 Ensure that the informed consent process and documentation for informed consent have been provided for convened IRB review, and request additional information if necessary;

2.2.2.3 Examine submissions for requests for waiver of informed consent, waiver of consent documentation, or HIPAA partial waiver request (ref. IRB SOP 3.15 Waiver, Alterations, and Exceptions to Informed Consent);

2.2.2.4 Review all informed consent documents submitted for IRB review for required and additional elements, as appropriate;

2.2.2.5 Request additional information, as needed, for the protocol or informed consent document and correspond with the investigator requesting such information.

2.2.3 **Minor Modifications: Expedited Review of Previously Approved Research**

The IRB chair reviews minor modifications to the informed consent documents by the expedited procedure or refers modification requests for review to the convened IRB (ref. IRB SOP 2.03 Proposed Modifications/Amendments in Previously Approved Research Studies).

2.2.4 **Consent Observation**

The IRB chair may request that an observation of obtaining informed consent be performed by a member of the IRB staff or by a third party.

2.3 **Convened IRB Responsibilities**

At the time of initial IRB submission, the convened IRB shall review the consent process including:

2.3.1 Review of all informed consent documents required and additional elements, as appropriate;

2.3.2 Review the nature of the proposed participant population including targeted vulnerable populations;

2.3.3 Assess whether the purpose, risks, and benefits in the informed consent agree with the research protocol;

2.3.4 Review the circumstances under which the consent process will occur including:

2.3.4.1 Personnel involved;

2.3.4.2 Manner and setting, and any waiting period involved;

2.3.4.3 Opportunities for exchange of information between the participant and the individual obtaining consent.

2.3.5 Consider additional protections for informed consent for vulnerable populations including:

2.3.5.1 Plans for non-English speaking participants, involving a translator fluent in both English and participant's language;

2.3.5.2 Determining that requests for the use of an LAR is justifiable for the subject population, if applicable;

2.3.5.3 Incorporation of consent procedures in accordance with policies and procedures for pregnant women and fetuses, and decisionally impaired adults, as applicable.

2.3.6 Consider any other procedures proposed to minimize coercion and undue influence;

2.3.7 Approval of the research only if the IRB determines and documents that the requirements for informed consent are satisfied by confirming the following, unless the IRB waives or alters informed consent:

2.3.7.1 The informed consent process appears to be legally effective;

2.3.7.2 The informed consent process provides the participants ample opportunity to consider whether or not to participate;

2.3.7.3 The information given to the participants will be in language understandable to participants;
2.3.7.4 For non-English-speaking participants, translation of informed consent documents is certified by qualified personnel;
2.3.7.5 No exculpatory language is present in which the participant waives or appears to waive legal rights;
2.3.7.6 The informed consent process minimizes risk to coercion and undue influence including use of additional protections for vulnerable targeted populations;
2.3.7.7 The informed consent disclosures accurately portray the purpose, risks and benefits of the study.

2.3.8 Approval of the research only after determining that the requirements for documentation of informed consent are satisfied, unless the IRB waives documentation of informed consent, by assuring that:
2.3.8.1 The written informed consent document embodies the elements and disclosures of informed consent;
2.3.8.2 The informed consent provides for the document to be signed and dated by the participant, witness, and (if applicable) the investigator;
2.3.8.3 The study gives the participant adequate time to read the consent;
2.3.8.4 The consent states that a signed copy will be given to the person signing the form.

2.3.9 Review all amendments to the informed consent process or documentation of informed consent process that potentially changes the risk-benefit ratio for participants and determines whether the information affects participants' willingness to participate and, if so, the appropriate manner to inform participants.

2.4 IRB Office Responsibilities

2.4.1 Prepare and send correspondence as directed by the IRB chair requesting more information or granting approval of informed consent documents reviewed by expedited review;
2.4.2 Prepare and send correspondence as outlined in the IRB meeting minutes granting approval or requesting modifications to the informed consent document reviewed by the IRB;
2.4.3 Issue the informed consent documents with the current IRB approval stamp; the informed consent bearing the approval stamp must be used when consenting participants;
2.4.4 Provide the stamped, approved informed consent documents and appropriate correspondence to the investigator and/or their designee; and
2.4.5 Manage scheduling of any observation of obtaining informed consent as directed, with the investigator and reports findings to the IRB; reporting shall include assurance that no patient identifiers are contained in the report.

2.5 Informed Consent Posting

The Revised Common Rule (i.e., 2018 Requirements) at 45 CFR 46.116(h) requires that for each clinical trial conducted or supported by a federal department or

agency, one IRB-approved consent form used to enroll subjects must be posted on a publicly available federal website by the awardee or the federal department or agency component conducting the trial.

2.5.1 **Purpose**

The purpose of this requirement is to provide increased transparency of the consent forms being used and, over time, improve the quality of consent forms.

2.5.2 **Clinical Trial**

A clinical trial is defined as a research study in which one or more human participants are prospectively assigned to one or more interventions, which may include placebo or other control, to evaluate the effects of the interventions on biomedical or behavioral health outcomes (ref. 45 CFR 46.102(b)). Posting of one approved informed consent form is required for two categories of clinical trials:

2.5.2.1 Category 1

Nonexempt clinical trials (as defined by 45 CFR 46.102(b)) conducted or supported by HHS and initially approved by an IRB on or after January 21, 2019.

2.5.2.2 Category 2

Nonexempt clinical trials (as defined by 45 CFR 46.102(b)) conducted or supported by HHS and initially approved by an IRB before January 21, 2019 which also continue on or after January 21, 2019, and for which both of the following are true:

2.5.2.2.1 An institution transitions the clinical trial to comply with the 2018 Requirements in compliance with the transition provision (45 CFR 46.101(l)), and

2.5.2.2.2 The transition determination was documented and dated by the IRB or institution before the timeframe specified in 45 CFR 46.116(h)(3) has passed (i.e., the clinical trial is closed to recruitment and 60 or fewer days before the last protocol-required study visit by any subject enrolled in the protocol).

2.5.3 **Implementing the Informed Consent Posting Policy**

The Revised Common Rule requires clinical trials to post one IRB-approved version of a consent form that has been used to enroll participants on a public federal website designated for posting such consent forms.

When must a consent form be posted for clinical trials initially approved on or after January 21, 2019?

The 2018 Requirements state that a consent form must be posted to a designated federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required

by the protocol. While a consent form could be posted before a clinical trial closes recruitment, it does not satisfy the requirement at 45 CFR 46.116(h). If a consent form is posted before a clinical trial closes recruitment, it would have to be re-posted after the clinical trial closes recruitment in order for 45 CFR 46.116(h) to be satisfied.

Who may post the consent form?
Under the 2018 Requirements, "the awardee(s)" or a federal agency component(s) conducting a trial is (are) responsible for compliance with this posting requirement. For the purposes of 45 CFR 46.116(h), the Office for Human Research Protections (OHRP) interprets the term "awardee" to refer to the institution (or one of the institutions) engaged in the HHS-conducted or HHS-supported research. However, the posting responsibility may also be assigned to an investigator or IRB staff person, among others. Ref. OHRP Informed Consent Posting Instructions

2.5.3.1 Uploading an Informed Consent Form

At this time, two federal websites have been identified as locations for informed consent forms posting, satisfying 45 CFR 46.116(h). *(Back to 2.5 Informed Consent Posting)*

ClinicalTrials.gov
An IRB-approved version of the form can be uploaded to the ClinicalTrials.gov study record. (Note that the website ClinicalTrials.gov does not accept non-English documents.) Specific instructions on how to register with ClinicalTrials.gov and upload clinical trial informed consent forms may be found at Submit Studies.

Regulations.gov
An IRB-approved version of the form can be uploaded to Regulations.gov, Docket ID: HHS-OPHS-2018-0021:

- Submit the informed consent form as a comment to the appropriate docket folder;
- Instructions for uploading can be found on the OHRP website;
- Maintain a copy of your Regulations.gov receipt.

The awardee or the federal department or agency conducting the clinical trial may select either website to satisfy the posting requirement.

2.5.4 Redacting Confidential Information on the Consent

If the consent form has information that should not be publicly available, the federal department or agency supporting the research may permit or require redactions of proprietary, sensitive, or non-public information in the

consent form (e.g., confidential commercial information). The Administrative Grant Specialist of the federal department or agency should be contacted to inquire about the process for redacting such information from the informed consent form prior to posting.

2.5.5 **Exceptions to the Posting Requirement**
The Administrative Grant Specialist of the Federal department or Agency should be contacted to request an exception to the posting requirement.

3.0 REFERENCES

3.1 IRB Standard Operating Procedures
- 3.1.1 SOP 3.15 - Waiver, Alterations, and Exceptions to Informed Consent
- 3.1.2 SOP 3.18 - Additional Safeguards for Individuals Without Decision-making Capacity
- 3.1.3 SOP 1.10 - Emergency Use of An Investigational Drug, Biological Product, or Device
- 3.1.4 SOP 2.03 - Proposed Modifications/Amendments in Previously Approved Research Studies

3.2 National Institutes of Health: Posting Clinical Trial Informed Consent Forms

3.3 ClinicalTrials.gov: Submit Studies

3.4 Code of Federal Regulations
- 3.4.1 U.S. Department of Health and Human Services (HHS)
  - 3.4.1.1 45 CFR Part 46, Subpart B
  - 3.4.1.2 45 CFR 46.109(b)
  - 3.4.1.3 45 CFR 46.109(e)
  - 3.4.1.4 45 CFR 46.111
  - 3.4.1.5 45 CFR 46.116
  - 3.4.1.6 45 CFR 46.116(a)
  - 3.4.1.7 45 CFR 116(c)
  - 3.4.1.8 45 CFR 46.116(d)
  - 3.4.1.9 45 CFR 46.116(f)(1)
  - 3.4.1.10 45 CFR 46.117
  - 3.4.1.11 45 CFR 46.117(c)(1)
  - 3.4.1.12 Waiver of Informed Consent Requirements in Certain Emergency Research at 61 FR 51531
- 3.4.2 U.S. Food and Drug Administration (FDA)
  - 3.4.2.1 21 CFR 50.20
  - 3.4.2.2 21 CFR 50.23(d)
  - 3.4.2.3 21 CFR 50.23(e)
  - 3.4.2.4 21 CFR 50.24
  - 3.4.2.5 21 CFR 50.25
  - 3.4.2.6 21 CFR 50.27
  - 3.4.2.7 21 CFR 56.109(c)
  - 3.4.2.8 21 CFR 56.109(d)
  - 3.4.2.9 21 CFR 56.109(f)
  - 3.4.2.10 21 CFR 56.111

3.5 Office for Human Research Protections
- 3.5.1 Informed Consent Posting Instructions
- 3.5.2 Uploading a Clinical Trial Informed Consent form to Regulations.gov

3.6 AAHRPP Domains and Elements
- 3.6.1 II.3.F.
- 3.6.2 II.4.B.
- 3.6.3 III.1.F.