I. **INTRODUCTION:** The ethical conduct of clinical investigations is based upon the voluntary consent of the study participant who has been appropriately informed about a study's risks and benefits. It is the responsibility of the investigator to ensure that all federal and state regulations have been met through the language of the Informed Consent Document (ICD), and that Informed Consent itself has been properly obtained from the study participant or the participant's legally authorized representative.

Each potential participant or their legally authorized representative (LAR) must provide legally effective Informed Consent prior to joining a research study, unless otherwise approved by the Institutional Review Board (IRB) of Record.

II. **PURPOSE AND SCOPE:** This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and ethical requirements for developing the paper and/or electronic ICD and for appropriately obtaining and documenting the participant's Informed Consent by in-person or Remote process.

The intent of this SOP is to describe the following responsibilities of the Principal Investigator (PI) and study team members to whom the PI has delegated Informed Consent duties:

- Process for preparing an ICD – either paper or electronic
- IRB submission
- Process for obtaining Informed Consent for research participants involved in any clinical research conducted by Loyola University Chicago (LUC) either in-person or remote, verbal or written
- Process for obtaining Informed Consent and/or assent for research involving minors.
- This SOP also specifies the conditions for exceptions from the general requirements for obtaining Informed Consent and for emergency research.

This SOP applies to all clinical studies that utilize an Informed Consent, including studies that are initiated by the PI and are sponsored by LUC. An IRB of Record other than LUCHSC IRB may have policies relating to electronic consenting that are beyond this SOP. Any additional procedures required by an IRB of Record or the study's sponsor must be followed.

III. DEFINITIONS AND ABBREVIATIONS

CFR – Code of Federal Regulations
Confidentiality - Prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or of a participant's identity.
Consenter – A study team member who has been delegated by the PI to obtain Informed Consent from a potential research participant. This may be:
(a) the PI, sub-investigator or
(b) a person who is:
1. qualified to explain the study and the medical procedures (if applicable);
2. formally delegated this responsibility by the PI; and
3. approved by the LUCHSC IRB to perform study activity.

eIC – Electronic Informed Consent also referred to as "eConsent"
eICD – Electronic Informed Consent Document
ICD – Informed Consent Document
Impartial witness - A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, and who attends the Informed Consent process. Trinity Health recommends this person complete human subjects protection training.
Informed Consent - A process by which a participant voluntarily confirms his or her willingness to participate in a study, after having been informed of all aspects of the study that are relevant to the

participant's decision to participate. Informed Consent is documented by means of a written, signed, and dated ICD.
Institutional Review Board (IRB) - An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a research study by, among other things, reviewing, approving, and providing continuing review of studies, of protocols and amendments, and of the methods and material to be used in obtaining and documenting Informed Consent of the study participants.
LAR - Legally Authorized Representative: An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective participant, to the participant's participation in the research study.
LUCHSC IRB – Loyola University Chicago Health Sciences Campus Institutional Review Board. The LUCHSC IRB is the IRB of record for research conducted at LUC HSC, Loyola University Medical Center, Gottlieb Memorial Hospital, and MacNeal Hospital.
REDCap - Mature, secure web application for building and managing online surveys and databases. The REDCap platform can support processes that are 21 CFR part 11 compliant.
Remote consenting - Consent process when the Consenter and potential participant or LAR are not at the same location
Research Channel-LUCHSC portal that houses study related documents including IRB approval letters, currently approved IRB Informed Consent, research amendments and adverse events related to specific studies.
Study team members- Consists of a Principal Investigator, Sub-Investigators, research nurses, clinical protocol coordinators or designee who is delegated to perform activities on a study.
Vulnerable subjects - Individuals whose willingness to volunteer in a clinical research study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable participants include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent. 45 CFR Part 46 defines pregnant women, human fetuses, neonates, prisoners, and children as vulnerable populations.

IV. Procedure

a. Drafting or Adapting the ICD and/or eICD for LUCHSC IRB Review and Approval

i. Based upon the protocol and additional relevant documentation, if applicable, such as the protocol's model consent template, prepare an ICD utilizing the locked LUCHSC IRB Informed Consent template form found in the Research Channel.
ii. Verify that all protocol required and additional elements of the ICD are incorporated in the Loyola ICD by using the Informed Consent format and content checklist. Maintain the required language in the LUCHSC IRB Informed Consent template in the harmonized ICD.
iii. If applicable, submit the harmonized draft ICD to the Sponsor for review. Negotiate with the Sponsor until they approve a version for local IRB submission.
iv. Prepare the initial IRB submission.
    1. Include the final harmonized ICD with the IRB submission.
    2. If the study intends to utilize an electronic Informed Consent document (eICD), the IRB must first approve the use of an electronic consent process (eConsent). Details related to the eConsent process (eIC) must be included in the study protocol for the IRB review prior to approval. eConsent is to be setup on a per project basis.

3. If the study intends to utilize remote consent, details related to the remote consent process must be included in the study protocol or supplementary documentation included with the IRB application.
4. If the study intends to utilize verbal consent, as may be the case for participant populations who are expected to be on droplet precautions or other infection prevention restrictions or where remote consent is expected and the participant population may not have access to the technology needed for written remote consent, details related to the verbal consent process must be included in the study protocol or supplementary documentation included with the IRB application.

v. The IRB may modify or request the study team modify the ICD before it is approved. Review all changes in the final approved version.
vi. If applicable, forward the ICD and IRB approval letter to the Sponsor. Note any IRB required changes to the ICD.
vii. If eConsenting is approved by the IRB, the Study Team may proceed with building out or requesting build out of the eICD in the most current 21 CFR part 11 compliant version of REDCap. The electronic version of the consent in REDCap must be identical to the IRB approved consent located in the Research Channel. The Consenter will receive access to REDCap project to utilize eConsent function.

b. Obtaining Written Informed Consent Utilizing In-Person Consenting Process

i. The Consenter will confirm he/she is using the current IRB-approved ICD located under the study's LU number in the Research Channel, whether in paper or in REDCap.
ii. If required by the IRB, the Consenter will ensure the impartial witness is present when he/she approaches the potential participant or LAR for the consent process.
iii. The Consenter will introduce the study to the potential participant or LAR and:
    1. If using a paper ICD, will provide the potential participant or LAR with a copy of the ICD to read and review.
    2. If using eConsent, will provide the potential participant the option to either use an ICD (paper copy) or an eICD. If the potential participant or LAR chooses to use the eICD, the Consenter will assist with navigating the eICD on a computer screen or electronic tablet. If the study requires eConsent and the potential participant or LAR is not willing to complete the eConsent process, he/she may not be able to participate in the study.
iv. The Consenter will ensure that:
    1. The potential participant or LAR is given sufficient time to review the consent document, ask any questions, and have their questions answered by a member of the study team. If the Consenter is not a medical practitioner, she/he will ensure that an authorized medical practitioner is available to answer the potential participant's or LAR's questions as necessary.
    2. The potential participant or LAR verbalizes an understanding of the study requirements, the risk/benefits, and that he/she may withdraw from study participation at any time.
    3. The ICD or eICD is in a language understandable to the potential participant or LAR (the LUCHSC IRB *Policy and Procedure on Consenting Limited English Proficient Research Participants* will be followed if applicable).
    4. The potential participant or LAR makes no changes to the ICD or eICD.
    5. The participant or LAR signs and dates the ICD or eICD voluntarily.

6. All signature/initial lines/check boxes on the ICD or eICD are appropriately completed, including the Consenter and impartial witness signature, if applicable.
7. A copy of the signed and dated ICD is provided to the participant or LAR.
    a. If using an eICD, a copy of the signed and dated eICD must be printed and provided to the participant or LAR, or emailed to the participant or LAR according to their preference. Before emailing, the Consenter will confirm the potential participant or LAR permits the ICD to be sent to their specified email address as doing so may reveal the potential participant's medical condition.
8. If study activities take place in Loyola University Medical Center (LUMC), the ICD is uploaded into Epic according to SOP PAT-001: *Research Consent Forms in Epic*.
9. The signed original ICD or eICD is printed and kept in the research study file. It is retained with the study documents for the duration of record retention period. If the original ICD or eICD is inadvertently destroyed, a copy of the scanned version will be printed and filed along with a Note to File documenting why the original ICD is unavailable.

c. Obtaining Written Informed Consent Utilizing Remote Consenting Process

i. The Consenter will confirm the potential participant or LAR is willing to utilize a remote consent process.
    1. If using a paper ICD,
        a. The ICD may be mailed to the potential participant or LAR.
        b. The ICD may be emailed to the potential participant or LAR.
            i. The Consenter will confirm the potential participant or LAR has access to a smartphone, tablet or computer with Wi-Fi or cellular internet connectivity, an email address to receive the ICD, and a printer or electronic signature software.
            ii. The Consenter will confirm the potential participant or LAR permits the ICD to be sent to their specified email address as doing so may reveal the potential participant's medical condition.
            iii. If the potential participant or LAR does not have access to the technology required for remote consenting using an emailed ICD, this approach cannot be used.
    2. If using an eICD,
        a. The Consenter will confirm the potential participant or LAR has access to a smartphone, tablet or computer with Wi-Fi or cellular internet connectivity and an email address to access and complete the eICD.
        b. The Consenter will confirm the potential participant or LAR permits the link to the eICD to be sent to their specified email address as doing so may reveal the potential participant's medical condition.
        c. If the potential participant or LAR does not have access to the technology required for remote consenting using the eICD, this approach cannot be used. Paper ICD may be used in-person or under an IRB approved alternative consenting process, if the lack of technology does not disqualify the potential participant from the study.

ii. The Consenter will confirm he/she is using the current IRB-approved ICD located under the study's LU number in the Research Channel, whether in paper, electronic copy, or in REDCap.
iii. The Consenter will provide a copy of the ICD or eICD to the potential participant or LAR.
    1. If using paper ICD, the Consenter will mail or email the ICD to the potential participant or LAR. If emailed, the potential participant or LAR will print the ICD or, if they have access to electronic signature capabilities, may open the ICD electronically. The Consenter will also have a copy of the current ICD in his/her possession to reference.
    2. If using eConsent, using the REDCap platform, Consenter will email or text the URL link of the eICD to the potential participant or LAR. The Consenter will also have a copy of the current eICD in his/her possession to reference.
iv. The Consenter will contact the potential participant or LAR over the phone or video conference to confirm that they are able to open and view the ICD or eICD and to begin the Remote consenting process.
v. If an Impartial witness is required, the Consenter will confirm the impartial witness is present on the phone line or video conference.
vi. The Consenter will request the potential participant or LAR to conduct the eIC discussion in a private location to help ensure privacy and confidentiality.
vii. The Consenter will ask each individual on the phone line or video conference to introduce his/her self by name and, for those on the study team and the impartial witness, by title.
viii. The Consenter will verify the potential participant's or LAR's identity.
    1. If the potential participant is a patient at LUMC and the Consenter has permissible access to the patient's medical record:
        a. The Consenter will verify the potential participant's identity by asking full name and date of birth and comparing to their medical record.
        b. The Consenter will verify the LAR's identity by asking the name, relationship to patient, and/or other information as documented about the LAR in the patient's medical record.
    2. If medical record verification isn't possible, the Consenter will request the potential participant's or LAR's photo identification, preferably government-issued, via email or by displaying during a video conference.
ix. The Consenter will verify the version date of the ICD/eICD with the potential participant or LAR.
x. The Consenter will ensure that:
    1. The potential participant or LAR is given sufficient time to review the ICD/eICD, ask any questions, and have their questions answered by a member of the study team. If the Consenter is not a medical practitioner, s/he will ensure that an authorized medical practitioner is available to answer the potential participant's or LAR's questions as necessary.
    2. The potential participant or LAR verbalizes an understanding of the study requirements, the risk/benefits, and that he/she may withdraw from study participation at any time.
    3. The ICD/eICD is in a language understandable to the potential participant or LAR (the LUCHSC IRB *Policy and Procedure on Consenting Limited English Proficient Research Participants* will be followed if applicable).
    4. The potential participant or LAR makes no changes to the ICD.
    5. The participant or LAR signs and dates the ICD/eICD voluntarily.

6. All signature/initial lines/check boxes on the ICD/eICD are appropriately completed.
    a. If using paper ICD, the participant or LAR will:
        i. Sign electronically and email the signed ICD to the Consenter.
        ii. Scan or take a picture of the printed, signed ICD and email it to the Consenter.
    b. The Consenter will print the signed ICD and sign it and have it signed by the impartial witness, if applicable.
7. For eConsenting, a copy of the signed eICD will be automatically saved in the eIC database and should be immediately accessible to the Study Team for review.
8. The Consenter will mail a printed copy or email an electronic copy of the ICD/eICD to the participant or LAR depending on their preference.
9. If study activities take place in LUMC, the ICD/eICD is uploaded into Epic according to SOP PAT-001: *Research Consent Forms in Epic*.
10. The signed ICD/eICD is kept in the research study file. It is retained with the study documents for the duration of record retention period. If the signed ICD/eICD is inadvertently destroyed, a copy of the scanned version will be printed and filed along with a Note to File documenting why the original ICF is unavailable.

xi. In the case of technical difficulties with the eIC platform, Informed Consent must proceed using a paper ICD.

d. Obtaining Verbal Informed Consent

i. If approved by the IRB, if the potential participant or LAR is unable to provide written consent, he/she may provide verbal consent.
ii. The Consenter completes the steps for in-person or remote consent as described in sections (b) and (c) above with the following exceptions:
    1. An impartial witness is required.
    2. If the potential participant or LAR gives verbal consent, the Consenter writes "verbally consented [over the phone/via teleconference/through hospital room door]" on the participant or LAR signature line.
iii. The participant or LAR will sign the ICD/eICD when they are able to provide written consent for continued participation.

e. Documentation of Informed Consent Process

i. Document the following steps in a source document. If study activities will take place in LUMC, the documentation should be in Epic.
    1. The names of those involved in the consent process, including as applicable the Consenter, participant, LAR and impartial witness.
    2. If the participant or LAR was consented utilizing a written, eConsent, remote, and/or verbal process. If remote or verbal, the reason written or in-person consent could not be obtained.
    3. The Consenter explained the study and the participant or LAR verbalized understanding.
    4. Any questions were answered.
    5. The participant or LAR was given adequate opportunity to consider all available options.
    6. The participant or LAR agreed to participate.
    7. The date the ICD/eICD was signed. If required by the sponsor or study design, a notation of the time signed will also be documented.
    8. A copy of the signed ICD/eICD was given to participant or LAR.

9. No study activities were conducted prior to the ICD or eICD being signed (unless otherwise permitted by the IRB).

ii. A template note incorporating the items above can be used as a guide to document the Informed Consent process.

iii. If verbal consent was initially obtained or if an LAR initially provided consent, and at a later date the participant provides written consent, the subsequent consent process is to be documented as well.

f. Revisions to the ICD or eICD

i. In the event that the ICD or eICD needs to be revised during the course of the study due to a protocol amendment, update to the Investigator's Brochure, or other reason, the study team will obtain IRB approval of the revised ICD or eICD prior to implementation, except in the case of an immediate participant safety concern. An ICD/eICD addendum (abbreviated consent outlining ICD/eICD changes) may be utilized for participants already on study, if approved by the IRB.

ii. A participant or LAR must be re-consented if changes to the ICD or eICD indicate a change in the risk-benefit ratio, new risks, any change that might relate to the participant's or LAR's willingness to continue participation in the study, or if directed by the IRB.

iii. During the re-consenting process, the same requirements for obtaining written or verbal informed consent remotely or in-person are followed.

iv. To continue in the study, the participant or LAR must voluntarily agree to continue participation. The participant or LAR must sign and date the revised ICD or eICD or consent addendum.

v. The participant or LAR will be provided with a copy of the revised ICD, eICD, or consent addendum. The original signed revised ICD or eICD or addendum will be filed in the study file. **Earlier, superseded signed ICDs/eICDs will be retained in the study file**.

vi. The FDA and LUCHSC IRB do not require participants to be re-consented if they have completed active participation in a study. Participants will be re- consented if information is received that affects the risks to the research participants on the study.

vii. Re-consenting will typically take place at the participant's next scheduled study encounter, although the PI or member of the study team may verbally communicate the ICD changes to the participant or LAR through a phone call prior to their visit. If the study is IRB approved for remote consent, the procedures listed under the section, *Obtaining Written Informed Consent Utilizing Remote Consenting Process* may be followed.

g. If the PI or any research study staff discovers that an expired or incorrect version of the ICD or eICD was used for a participant still actively participating in the study, s/he will:

i. Notify the LUCHSC IRB and the study Sponsor, if applicable, of non-compliance within 10 business days of when the staff member becomes aware of the event and follow the IRB's recommendation on how to proceed.

ii. If it is determined that the participant will need to be re-consented, the study team member will:

1. Contact the participant or LAR and explain the changes in the ICD or eICD.
2. If the participant or LAR wants to continue in the study, complete the signing of the correct ICD/eICD as soon as feasible.
3. Instruct the participant or LAR to use the present date when signing the correct ICD or eICD version.
4. Provide a copy of the signed correct ICD or eICD version to the participant or LAR.

5. Maintain both signed versions of the ICD or eICD in the files.
6. Write an explanatory Note to File so that future auditors will understand why two signed ICD or eICDs for the same participant are present in the file.

iii. If the study staff can't contact the participant or LAR or they have been lost to follow up, the study staff creates a Note to File to document the dates and methods by which the attempts to reach the participant or LAR were made.

h. **Obtaining Informed Consent and/or Assent for Research Involving Minors**

i. Consent:

1. Consult with the IRB regarding state and local laws for the consent of minors.
2. If the potential participant is considered to be a legal minor, obtain consent from one or both parents, or legal guardian as instructed by the IRB.
3. Follow all procedures for obtaining and documenting the Informed Consent process as outlined above.
4. Provide a copy of the Informed Consent document to the parent(s) or legal guardian(s).

ii. Assent:

1. Consult with the IRB regarding their requirements for the assent of minors.
2. Utilize the IRB optional verbiage form, to be used by children, for their verbal or written consent for their participation in the study that describes the risks and benefits in age-appropriate language.
3. Follow all procedures for obtaining and documenting the Informed Consent process outlined above.
4. Provide a copy of the Informed Consent form to the child and parent (s) or legal guardian(s).

i. Waiver of Informed Consent in Emergency Situations

i. Provide the IRB with documentation from the investigator and the second physician within 5 working days of the emergency use of the test article.
ii. Notify the sponsor as soon as possible of the above actions.

Emergency use is defined as the use of an investigational test article with a human subject in a life-threatening situation and in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. This is expected to be a rare event.

When administering an investigational test article, requirements differ depending on your ability to obtain informed consent:

Circumstance 1: The patient is able to give informed consent and the treatment must be instituted prior to the next convened meeting of the IRB. In this circumstance the IRB Chair/designee is to be notified of the use of the test article prior to its administration.

The IRB Chair/designee will meet with or discuss the treatment plan with the physician prior to confirm that:

a) A life-threatening situation and/or a severely debilitating disease or condition exists requiring treatment with the test article before the next convened IRB meeting;
b) No standard acceptable treatment is available;
c) Insufficient time is available to obtain IRB approval at a convened meeting.

Life-threatening: diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subject must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating: diseases or conditions that cause major irreversible morbidity, such as severely debilitating conditions include blindness; loss of arm, leg, hand or foot; loss of hearing; paralysis or stroke: Prospective informed consent must be obtained and the physician must work with the provider of the test article sponsor to have the test article. Notification of the FDA will usually be managed by the provider and an individual physician sponsored IND may be obtained.

The investigator will create an informed consent that contains the required elements of consent along with the HIPAA authorization. The patient will sign the consent document prior to the intervention.

The physician will administer the test item and will submit the single use with the appropriate protocol, consent document and a statement of the emergency as a New Project Submission" and indicate the number of participants as "1". The Board will review the information and will issue an approval. In this case the approval means that the statutory requirements of use of a test article without prior IRB review and approval were met. Upon approval the project will be closed to new participant enrollment.

The emergency use of a test article must be reported to the IRB within 5 working days. The Chair of the IRB or designee will review all reports for emergency use of a test article. This information will be presented at the next convened IRB meeting.

Circumstance 2: The patient is not able to give informed consent, and time does not exist to obtain surrogate consent and the treatment must be instituted prior to the next convened meeting of the IRB.

In this circumstance we require a statement from a physician not participating in the treatment that:

a) the subject is confronted by a life-threatening situation necessitating the use of the test article;
b) that consent could not be obtained from the patient or the patient's representative because:
    i) of their medical condition;
    ii) the intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible;
c) there is no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of a subject.

If time does not permit independent physician verification of a-c above then the test article can be administered and the verification performed within 5 days and reported to the IRB.

The physician will administer the test item and will submit the single use with the appropriate protocol, and independent physician verification and a statement of the emergency as a New Project Submission" and indicate the number of participants as "1".

The Board will review the information and will issue an approval. In this case the approval means that the statutory requirements of use of a test article without prior IRB review and approval and without obtaining prospective consent were met. Upon approval the project will be closed to new participant enrollment.

The emergency use of a test article must be reported to the IRB within 5 working days. The Chair of the IRB or designee will review all reports for emergency use of a test article and determine whether the circumstances met FDA regulations. This information will be presented at the next convened IRB meeting.

The Board is notified of the use of the test article. It is to be noted that the notification of the IRB does not constitute IRB approval of the use of the article since there is no statutory basis for the Chairman to approve the prospective, single use of the test article.

Anticipated subsequent use requires a research protocol and consent and prior IRB review and approval before any further use of the test article. It is anticipated that the patient will be notified at the earliest opportunity of the use of the test article.

V. References and Applicable Regulations and Guidelines:

LUCHSC IRB Reference Guide for Research Investigators and Staff (Version 1.0, May 14, 2014)
LUCHSC IRB Policy and Procedure on Consenting Limited English Proficient Research Participants
SOP PAT-001: Research Consent Forms in Epic
21 CFR 50.25: Elements of Informed Consent
21 CFR 56.109: IRB review of research
21 CFR 56.111: Criteria for IRB approval of research
21 CFR 312.54: Emergency research under 50.24 of this chapter
21 CFR 312.60: General responsibilities of investigators
21 CFR 312.62: Investigator recordkeeping and record retention
45 CFR 46.116: General requirements for Informed Consent
FDA Guidance: A Guide to Informed Consent- guidance for Institutional Review
Information Sheet: Boards and Clinical Investigators Nov 2014
FDA and OHRP harmonized final guidance “Use of Electronic Informed Consent in Clinical Investigations”

VI. APPROVALS

1/12/21

Richard K. Freeman, MD, MBA, FACS — Date
LUMC Regional Chief Clinical Officer

DocuSigned by:
Meharvan Singh
9960F18DC5B43B...
1/14/2021

LUC Vice Dean of Research (or designee) — Date