1. OBJECTIVE

To ensure that the Principal Investigator (PI) and all research team members assisting in the conduct of clinical research are informed about their obligations and responsibilities as they pertain to Good Clinical Practices (GCP), the investigational plan, applicable regulations, guidance, and institutional policies. This Standard Operating Procedure (SOP) applies to the written procedures followed by all members of a clinical research team involved in the conduct of human subjects' research at LSU Health New Orleans, including the Health Sciences Center (HSC), the Stanley S. Scott Cancer Center (SSSCC) and the Healthcare Network (HN), hereafter called the investigational site. These detailed instructions promote compliance in conducting clinical research.

SOP 2.06 describes the process for fulfilling the regulatory and ethical requirements for developing and writing the Informed Consent Form (ICF) for clinical research; and the process for obtaining informed consent of subjects for clinical research.

2. RESPONSIBILITY

The HSC, SSSCC, and HN Clinical Trials Offices develop, implement, and maintain SOPs. The need to write a new or revise an existing SOP is based upon changes to federal regulations, guidelines, institutional policies, or procedures. These documents will be provided to departments and research teams conducting human subjects' research. Departments or research teams may develop additional research SOPs or a Research Procedure Addendum (RPA) to expand on an existing SOP, however this need should be limited.

The PI is ultimately accountable for all clinical research activities and is responsible for the appropriate delegation of tasks to individuals with adequate training and education to perform such tasks. It is the responsibility of all members of the clinical research team involved in supervising, managing, or conducting study-related activities to follow the SOPs. The clinical research team may include but is not limited to the following members:

Research Team Members

Principal Investigator (PI)	Clinical Research Coordinator (CRC)
Sub-Investigator (Sub-I)	Other Research Staff
Clinical Research Nurse Coordinator (CRNC)	Administrative and Support Staff

3. DEFINITIONS

Assent: A child's affirmative agreement to participate in research.

Coercion: Persuasion (i.e., of an unwilling person) to do or agree to something by using obvious or implied force or threats.

Confidentiality (*Regulatory Perspective*): The prevention of disclosure, other than to authorized individuals, of a subject's data or medical information. Privacy concerns people, whereas confidentiality concerns data.

HIPAA Authorization: A detailed document that gives covered entities permission to use protected health information for specified purposes, which are generally other than treatment, payment or healthcare operations, or to disclose protected health information to a third party specified by the individual.

Impartial Witness: A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject to affirm the completeness of the consent process.

Informed Consent: The process by which a subject voluntarily confirms his or her willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to the subject's decision to participate.

Informed Consent Form (ICF): The form on which the process of conducting and achieving informed consent from potential study subjects is documented.

IRB of Record: The IRB that is responsible for the ethical review of Human Research on behalf of an institution/organization or individual investigator.

Legally Authorized Representative (LAR): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures(s) involved in the research.

Notice of Privacy Practices (NPP): This notice describes how subject's medical/dental information may be used and disclosed and how subject can get access to this information.

Privacy: The right to protect a subject from intrusion and for the subject to control access to themselves. *Privacy concerns people, whereas confidentiality concerns data.*

Short Form: A written document stating that the elements of informed consent required by regulation have been presented orally to the subject or the subject's legally authorized representative in a language understandable to the subject or the subject's legally authorized representative.

Subject: An individual who participates in a clinical study, either as a recipient of the investigational drug or medical device or as a control. The terms subject and participant are used synonymously.

Vulnerable Subject: An individual whose willingness to volunteer in a clinical 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.

Please refer to the SOP Glossary document for other detailed definitions of commonly used clinical research terminology.

4. PROCEDURES

A. Informed Consent Form Development

a. Drafting and Developing the Informed Consent Form

Prior to implementation of a trial the PI must have IRB approval of the written ICF document and any other written information provided to subjects.

Based upon the protocol, the Investigator's Brochure (if applicable), and templates provided by the LSUHSC IRB or alternate IRB of record and the sponsor (if applicable), the PI and delegated research team members will prepare a draft ICF.

IRB provides templates for ICFs that contain all elements required by federal regulations and university policy. The PI and delegated research team members will verify that all required and appropriate elements of the ICF are included. These templates will be used to develop the informed consent document or to adapt the sponsor's informed consent document to meet the requirements of the IRB. If it is found that changes to the ICF are necessary, sponsor and/or PI approval are required prior to submitting to the IRB.

LSUHSC prefers use of our local-approved template; however, if the study team wishes to use the Sponsor template, LSUHSC required language must be embedded into the form.

The information that is given in the informed consent document to the subject or their legally authorized representative shall be in a language understandable to the subject or their representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

The ICF will be submitted to the IRB for review and approval along with any other required and applicable documents. The PI and delegated research team members, in collaboration with the sponsor, will make any necessary modifications to the consent form as requested by the IRB and re-submit for approval.

After the ICF has been approved by the IRB, the IRB approval letter, relevant communications, and approved ICF will be appropriately filed in the site's regulatory binder and saved electronically. Copies of the IRB approval letter and approved ICF will be sent to the sponsor for their records.

The ICF and any other written information provided to subjects will be revised whenever important new information becomes available that may be relevant to the subject's consent or that may be relevant to the subject's willingness to continue participation in the trial. Any revised written informed consent form document and written information will be submitted for IRB approval prior to use. of this SOP, if applicable.

b. Elements of the Informed Consent Form

Both the informed consent discussion and the written ICF, provided to subjects, may include but is not limited to the following elements:

General

- A concise and focused presentation of key information that includes only:
    - A brief description of the purpose of the study and procedures to be followed in lay terms,
    - A statement of the most important reason(s) a person may want to volunteer,
    - A statement of the most important reason(s)/risk(s) may not want to

volunteer for this study,
    - A statement clarifying that participation is voluntary and that rights and benefits are not dependent on participation, and
    - A contact person for a subject's questions, suggestions, or concerns
- The approximate number of subjects involved in the study.
- The probability for random assignment to each treatment.
- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
- For research involving more than minimal risk, an explanation as to whether any compensation, or any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained.
- A statement that the results of the research will be posted on ClinicaltTrials.gov.
- If the results of the trial are published, the participant's identity will remain confidential.
- For research involving biospecimens, a statement specifying, if known, whether the research will or could include whole genome sequencing.
- A statement that subject's biospecimens, even if de-identified, may be used for commercial profit and whether the subject will or will not share the commercial profit, if applicable.

Subject's Rights and Responsibilities

- The participant's responsibilities
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; contact information for the research team for questions, concerns, or complaints, and for someone independent of the research team for problems, concerns, questions, information, or input.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- A statement regarding whether clinically relevant research results, including individually relevant results, will be disclosed to the participant and if so, under what conditions.
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- Any additional costs to the subject that may result from participation in the research; and the amount and schedule of all payments to subjects.
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation.
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

Risks and Benefits

- A description of any reasonably-foreseeable risks or discomforts to the subject.
- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
- A description of any benefits to the subject or to others which may reasonably be expected of the research. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

Records Access and Review

- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and notes the possibility that the Food and Drug Administration may inspect the records.
- For research involving collection of identifiable information or biospecimens, either a statement that identifiers may be removed and after such removal, information and biospecimens could be used for future research or distributed to another researcher for future studies without additional informed consent, or a statement that subject information or specimens collected as part of the research, even if de-identified, will not be used or distributed for future use.
- A statement that the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the participant's original medical records for verification of clinical trial procedures and data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the participant's legally authorized representative is authorizing such access.

c. <u>Special Consent Circumstances</u>

The PI and delegated research team members will refer to LSUHSC IRB Policies & Procedures as well as the policies of the IRB of record (if other than LSUHSC IRB) for details on how to handle the following special consent circumstances:

- Child Assent
- Short Form Informed Consent
- Prisoner Consent
- Pregnant Women, Fetuses, and Neonates Consent
- Pregnant Partner Consent
- Expanded Access Use of Investigational Drugs, Biologics or Devices; Verbal Consent

B. Obtaining Informed Consent

Informed consent will be obtained by the PI or a delegated research team member only under circumstances that provide the prospective subject or the Legally Authorized Representative (LAR) sufficient opportunity to consider whether or not to participate, and that minimize the possibility of coercion or undue influence.

The PI and delegated research team member should comply with the applicable regulatory requirements, institutional policies, and to the ethical principles of human subjects' protection when obtaining and documenting informed consent of research subjects.

Individuals obtaining informed consent should be listed as personnel with the IRB, as well as listed on the Delegation of Authority log. These individuals will have appropriate training and education to perform such tasks.

The IRB application will clearly identify whether subjects recruited to the study represent a vulnerable population for which additional protections may need to be implemented as outlined by ORRP and IRB of record policies.

Prior to implementing the research study, the investigator will have the IRB approval of the written informed consent document and any other written information provided to subjects. Subjects will not be screened, recruited, or consented until final IRB approval of these documents has been received.

The approved documents will be updated to reflect approval date and document version by the research team members by the IRB of record. This will allow for version control to ensure the most recently approved consent form, HIPAA authorization, assent form and parental permission forms are used when consenting research subjects to the IRB approved research study. When the IRB of record is an IRB other than LSUHSC, all new and revised documents relevant to LSUHSC should be submitted to the LSUHSC IRB for acknowledgement, preferably within 30 days of lead IRB approval.

Special Considerations
Planned emergency research and expanded access use of investigational drugs, biologics, or devices for life-threatening conditions have special institutional requirements and processes that will be followed outside of the scope of this SOP, if applicable. Please refer to the reviewing IRB's policy on expanded access use of Investigational Drugs, Biologics or Devices.

a. Obtaining Consent
   The PI or delegated research team member will review and discuss details of the research study using the consent form as a guide. All basic elements of the consent form document, HIPAA authorization, Notice of Privacy Practice and any additional relevant information will be presented in detail to the prospective subject or the subject's LAR, if applicable.

   The information given to the subject or the representative shall be in a language understandable to the subject or the representative. No informed consent, whether verbal or written, will include any exculpatory language through which the subject or the subject's LAR is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

   The information presented should be written so that it is understandable to the potential

subject or the subject's LAR and should not include complex, technical, highly specialized language or medical jargon. The PI and delegated research team member should ensure that the potential subject or the subject's LAR do not feel coerced or unduly influenced to participate or to continue to participate in a research study. All consent discussions should take place in a private area with respect to the potential subject's privacy.

Before informed consent may be obtained, the PI or delegated research team member should provide the subject or the subject's LAR ample time and opportunity to read, inquire about the details of the study, and decide whether or not to participate in the study. The PI or delegated research team member will ensure the subject or the subject's LAR expresses understanding of information presented on the clinical research study, their participation is voluntary, and the subject can withdraw at any time without penalty. All questions about the study should be answered to the satisfaction of the subject. The investigational site should ensure the subject or the subject's LAR understands that, in order to participate in the clinical research study, the subject must be eligible per the protocol's inclusion and exclusion criteria.

Prior to any study related procedures, the PI or delegated research team member will obtain informed consent which will be documented by the use of a written consent form unless a consent waiver or waiver/alteration of documentation of consent has been previously approved by the IRB. The consent form document approved by the IRB will be signed and dated by the subject or the subject's LAR. Subjects/LARs who cannot write can indicate their consent by marking an "X" on the consent form. In this situation, a progress note in the subject's case history should indicate the reason for the lack of a signature. This form will also be signed and dated by the person obtaining consent and, if necessary, an impartial witness to the consent process.

All blanks on the consent form, Notice of Privacy Practices (if applicable) and HIPAA authorization form (if applicable) for subject name, subject initials, dates, signatures, yes/no check boxes for optional research procedures must be completed by the subject themselves or by the subject's LAR, if previously approved by the IRB. Delegated research team members ***may not*** complete these blanks for the subject.

The PI or delegated research team member will provide a copy of all signed forms to the subject or LAR.

A short form written consent document stating that the elements of informed consent, required by the FDA and institutional polices, may be presented orally to the subject or the subject's LAR if the ICF was not written in a language understandable to the subject or subject's LAR. When this method is used, there should be translator and , if the translator is a member of the research team, an impartial witness to the oral presentation. By signing the consent form, the witness attests that the information in the consent form, and any other written information, was accurately explained to and understood by the subject or the subject's LAR, and that informed consent was freely given by the subject or the LAR.

Informed consent is an ongoing process. Periodic review or confirmation of a subject's consent should be assessed by the PI and research team members.

b. Documentation of the Informed Consent Process

The original signed informed consent, HIPAA authorization form (if applicable), and Notice of Privacy Practices (if applicable) will be kept by the PI and delegated research team members, preferably in a binder or chart. All signed informed consent forms, HIPAA authorization forms (if applicable), and consent addendum forms (if applicable) of all subjects regardless of whether they are enrolled in the clinical research study will be kept in conjunction with the clinical research study essential documents and retained according to IRB of record policy.

The informed consent process will be documented by the PI or delegated research team member in a source document. The source document will outline the informed consent discussion with the subject or the subject's LAR.

c. Revisions to the Informed Consent

Informed consent is an ongoing process. Even in the absence of new information or changes to research procedures, periodic review or confirmation of a subject's consent should be assessed by the PI and research team members.

The informed consent form, and any other written information provided to subjects, may be revised whenever important new information becomes available or when administrative changes or general edits are needed. Revised informed consent forms and written information given to subjects must receive IRB approval prior to use.

If the new information raises awareness of an unacceptable increase in risk to the subject or eliminates an immediate hazard to the subject, the PI may deviate from the protocol and consent form document prior to review and documented IRB approval. The PI or delegated research team members may implement a deviation from, or a change in, the protocol to eliminate an immediate hazard to clinical research study subjects without prior IRB approval. The implemented deviation or change should be submitted to the IRB for review and approval, to the sponsor for agreement, and (if required) to the appropriate regulatory authorities within the required timeframe.

The subject or the subject's LAR will be notified of changes in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the research study. The communication of the changes in the consent form will be documented in the subject's research chart, if appropriate.

All above procedures and processes followed for obtaining initial consent apply to re-consenting subjects with a revised informed consent form.

d. Special Consent Circumstances

The PI and delegated research team members will refer to the IRB of record's Policies for

details on how to handle the following special consent circumstances where potential subjects may be deemed vulnerable or the type of research requires additional protections and processes:

- Child Assent
- Short Form Informed Consent
- Prisoner Consent
- Pregnant Women, Fetuses or Neonates Consent
- Pregnant Partner Consent
- Planned Emergency Research
- Expanded Access Use of Investigational Drugs, Biologics or Devices

5. APPLICABLE REGULATIONS AND GUIDANCE

LSU Health Guidance/Policy	Title
LSUHSC HRP Policies & Procedures	3.01 Conducting Review of New Applications
LSUHSC HRP Policies & Procedures	6.01 Informed Consent
LSUHSC HRP Policies & Procedures	6.02 Child Assent
LSUHSC HRP Policies & Procedures	6.03 Pregnant Partners
LSUHSC HRP Policies & Procedures	6.04 Verbal Informed Consent and Verbal HIPAA Authorization
LSUHSC HRP Policies & Procedures	7.01 Subject Population
LSUHSC Institutional Review Board	HIPAA & Research
LSUHSC Institutional Review Board	Collaboration with Local Institutions
LSUHSC Office of Compliance Programs	Privacy Requirements
LSUHSC Clinical & Translational Research Center (CTRC)	PM 205 SOP for Informed Consent
LSUHSC Clinical & Translational Research Center (CTRC)	PM 206 SOP for Consenting Non-English Speaking Subjects

Federal/International Regulation/Guidance/Policy	Title
21 CFR 50.20	General Requirements for Informed Consent
21 CFR 50.25	Elements of Informed Consent
21 CFR 50 (Subpart D)	Additional Safeguards for Children in Clinical Investigations of FDA-Regulated Products
21 CFR 56.109	IRB Review of Research

21 CFR 56.111	Criteria for IRB Approval of Research
21 CFR 312.54	Investigational New Drug Application: Emergency Research under 50.24
21 CFR 312.60	Investigational New Drug Application: General Responsibilities of Investigators
21 CFR 312.62	Investigational New Drug Application: Investigator Recordkeeping and Record Retention
21 CFR 812.100	Investigational Device Exemptions: General Responsibilities of Investigators
21 CFR 812.110(a)	Investigational Device Exemptions: Specific Responsibilities of Investigators
21 CFR 812.140(a)(3)(i)	Investigational Device Exemptions: Records
45 CFR 46.116	Final Rule
ICH E6(R2)	Guideline for Good Clinical Practices E6 Integrated Addendum
FDA Guidance for Industry	A Guide to Informed Consent – Information Sheet
FDA Guidance for Industry	Factors to Consider When Making Benefit-Risk Determinations for Medical Device Investigational Device Exemptions
FDA Guidance for Industry	FDA Decisions for Investigational Device Exemption Clinical Investigations
FDA Guidance for Industry	Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers

6. MATERIALS

6.1. Consent Documentation Note

6.2. Consent Process Checklist

Approved by:

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