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 2.18 describes the process for withdrawing a subject from further participation in research, either at the subject's request or at the PI's request.

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

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

4. PROCEDURES

A. Subject Withdraws Themselves from Further Participation in Research

a. <u>When a Subject Requests to Withdraw</u>

When a subject notifies the research team that they wish to withdraw from further participation in the research, it is the responsibility of the person who speaks with the subject to notify the PI or Sub-Investigator immediately of the conversation. It is the responsibility of the PI or Sub-Investigator to reach out to the subject within one (1) business day to discuss their decision to withdraw. While speaking with the subject, the investigator should ask if the subject is withdrawing from all components of the

research or would be willing to withdraw just from interventional components of the research and continue with other research activities. Under this circumstance, the discussion with the subject would distinguish between project-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the subject's information. When a subject's withdrawal request is limited to discontinuation of the interventional component of a research project, research activities involving other types of participation for which the subject previously gave consent may continue.

Documentation of the subject's request for withdrawal from further participation in research is required. Documentation should include:

- Date of withdrawl;
- The reasons for the withdrawal, if known; and,
- Whether the withdrawal was from all components of the research project or just the primary interventional component.

Also complete any forms or additional information required by the Sponsor and/or protocol.

Report the withdrawal of subjects to the Sponsor and the reviewing IRB. Depending on the circumstances, this information may be reported with the continuing review or may require prompt reporting as a Reportable Event.

b. Research Data Retention

When a subject withdraws from a project, the data collected on the subject to the point of withdrawal remains part of the project database and may not be removed. The consent document cannot give the subject the option of having data removed. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the project.

If a subject withdraws from the interventional portion of the project, but agrees to allow the investigator to continue other research activities described in the IRB-approved protocol and informed consent document that involve participation of the subject, such as:

- Obtaining data about the subject through interaction with the subject; or,
- Obtaining identifiable private information from the subject's medical, educational or social services agency records or from the subject's healthcare providers, teachers, or social worker.

If a subject withdraws from the interventional portion of a project and does not consent to continued follow-up of associated clinical outcome information, the investigator must discontinue the following activities involving that subject's participation in the research project.

- Interacting or intervening with the subject in order to obtain data about him or her for the research project;
- Obtaining additional identifiable private information about the subject for the research project by collecting or receiving such information from any source; and,
- Obtaining additional identifiable private information about the subject for the research project by observing or recording private behavior without interacting or intervening with the subject.

An investigator may review project data related to the subject collected prior to the subject's withdrawal from the project, and may consult public records, such as those establishing survival status.

c. HHS Conducted or Supported Research Subject to the HIPAA Privacy Rule
If a subject chooses to withdraw from future participation in research and also revokes authorization in writing for continued use or disclosure of his or her PHI that was already obtained in the research, analysis of that PHI may only continue to the extent necessary to protect the integrity of the research project.

B. Investigator Withdraws Subject from Further Participation in Research

If an investigator decides to terminate a subject's participation in a clinical trial without regard to the subject's consent, the investigator should ask the subject whether the subject is willing to continue participation in other research activities described in the IRB-approved protocol and informed consent document that involve participation of the subject, such as

- Obtaining data through interaction with the subject; or
- Obtaining identifiable private information from the subject's medical records or healthcare providers.

The investigator should explain to the subject the importance of obtaining follow-up safety data about the subject. If the subject agrees, research activities involving these other types of participation for which the subject previously gave consent may continue. The investigator should explain to the subject the reasons for this action and, as appropriate, other treatment options. For research greater than minimal risk the Investigators should document the determination to withdraw a subject from further participation. Documentation should include:

- Date of withdrawl;
- The reasons for the withdrawal, if known; and,
- Whether the withdrawal was from all components of the research project or just the primary interventional component.

Also complete any forms or additional information required by the Sponsor and/or protocol.

C. Subjects Lost to Follow-up

If a subject who was once actively participating in research is no longer attending study visits or is unreachable, the study team should take the following steps to contact the subject prior to considering the subject lost to follow-up:

a. Phone Contact
A member of the study team should attempt to contact the subject via phone three times, leaving voicemails as appropriate requesting a return call.

b. Certified Letter
If phone calls go unanswered or unreturned, a certified letter should be sent to the subject. The letter should include the following information:

- The IRB number, study title, and Principal Investigator name
- The date of the visit the subject missed that led to the phone calls
- The phone number the study team attempted to reach the subject at
- A study phone number the subject can call to reschedule the missed visit
- A request for the subject to notify the study team if they wish to withdraw
- A set number of days after which the subject will be withdrawn is no contact is made.

If no response is received to the phone calls and letter, then the subject should be considered lost to follow-up. A Note to File should be drafted outlining the loss to follow-up, including information about attempted contact. In addition, the Sponsor should be informed of the loss to follow-up and may require the subject's study status be updated or record the reason for study exit.

5. APPLICABLE REGULATIONS AND GUIDANCE

LSU Health Guidance/Policy	Title
LSUHSC HRP Policies & Procedures	6.01 Informed Consent
LSUHSC HRP Policies & Procedures	7.01 Subject Population
LSUHSC Institutional Review Board	HIPAA & Research
LSUHSC Office of Compliance Programs	Privacy Requirements

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 312.62	Investigational New Drug Application: Investigator Recordkeeping and Record Retention
21 CFR 812.140(a)(3)(i)	Investigational Device Exemptions: Records
ICH E6(R2)	Guideline for Good Clinical Practices E6 Integrated Addendum

FDA Guidance for Industry	Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers
FDA Guidance for Industry	Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials
OHRP/HHS Guidance	Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues

6. MATERIALS

6.1. Enrollment Log

Approved by:

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