Investigator Standard Operating Procedures

SOP No.: 103
Investigator Responsibility and Delegation of Authority

Author: Office of Human Research

Effective Date: Nov 18, 2016
Supersedes document dated: March 3, 2014

Last Reviewed on: Nov 2, 2016
Results of Review: Changes made and tracked

This SOP pertains to: Investigator and all other designated individuals involved in supervising, managing or conducting regulated human research activities within Memorial Healthcare System.

Responsibility for executing this SOP: Investigator and Designated Research Personnel

Approved By (Sign & Date):
Senior Vice President & Chief Medical Officer, MHS

Approved By (Sign & Date):
Chief Medical Research Officer, OHR

1 PURPOSE
This procedure defines the responsibilities of any Principal Investigator conducting FDA-regulated human subject research. It also identifies areas of accountability and the process for delegating or assigning the transfer of the Investigator’s responsibilities to other qualified individuals.

2 GENERAL INSTRUCTIONS AND RESPONSIBILITIES

a) The Investigator is the individual on record who assumes the authority and responsibility of all aspects in the conduct of a FDA or non-FDA regulated human subject research study and ensures that the clinical study is carried out in accordance with the protocol, ICH Good Clinical Practice (GCP) guidelines, all applicable regulatory requirements, and all applicable Memorial Healthcare System policies and procedures.

b) The Investigator is responsible for protecting the rights, safety, and welfare of study participants involved in the research.

c) The Investigator has the authority to delegate responsibility to individual members of the clinical research team based on their experience, training and qualifications; however, the Investigator is ultimately responsible for the overall conduct of the clinical study.

d) Key research personnel are defined as all individuals who contribute in a substantial way to the scientific development or execution of the study at or on behalf of Memorial Healthcare System or affiliated institutions. Typically, these individuals have doctoral or other professional degrees, although other individuals should be included if their involvement meets the definition of key personnel and they have been adequately trained on the specific task. All investigators and sub-investigators are considered key research personnel, as are individuals who consent subjects for research.

e) Key research personnel are responsible for carrying out their delegated responsibilities according to established policies, procedures and applicable regulatory requirements. The Principal Investigator may delegate additional duties as necessary. Commencement
of research related duties may only begin after the individual has received training on the protocol, completed institutional GCP requirements, and has been IRB approved (where applicable).

f) Non-key personnel are research personnel who either interact with subjects or access identifiable private health information but do not contribute in a substantive way to the scientific or scholarly development or execution of the study.

3 SPECIFIC PROCEDURES

3.1 Investigator Responsibilities

a) Follows standard operating procedures (SOP) to ensure that the conduct of FDA-regulated human subject research proceeds in compliance with ICH GCP Guidelines and all applicable regulations and that institutional requirements are met.

b) Ensures that controlled and non-controlled documents are developed, reviewed, approved, and modified in an accountable manner (Reference SOP 101 and 102).

c) Ensures that responsibilities and activities in the conduct of FDA-regulated human subject research that are delegated to others are understood by those who carry them out, and are delegated to individuals who are qualified by education, training, licensure, (if needed), and experience to carry out those responsibilities and activities, with appropriate documentation of that delegation. When the protocol requires specific qualifications of the individuals to perform certain tasks, the protocol should be followed.

d) Provides training on protocol requirements and documentation of the training.

e) Ensures that investigator(s) involved in IDE research directly supervise the placement and/or use of the device.

f) Follows training policies and procedures to provide all designated individuals with the opportunity to maintain and enhance their ability to carry out delegated responsibilities, and ensures all individuals engaged in clinical research have met their training requirements (Reference SOP 104).

g) Ensures that financial and professional conflicts of interest are recognized, reported to appropriate authorities, and any applicable management plans are followed per MHS guidelines.

h) Establishes criteria for selecting qualified non-agent contractors to conduct study-related activities when necessary and appropriate, and document those selection criteria and delegated responsibilities (Reference SOP 105) Investigator may consult with the OHR for assistance.

i) If the Investigator is also the Sponsor-Investigator:

   o Facilitates and coordinates effective written and oral communications with the FDA, including regulatory submissions, responses to questions and meetings, and maintains active FDA status with respect to conducting clinical studies using investigational drugs/biologics/medical devices, e.g., IND, IDE (Reference SOP 201) for the procedures.

   o Reviews and periodically evaluates the evidence relating to the safety and effectiveness of the investigational product and ensures that all relevant reports (e.g., clinical study reports, adverse event reports, safety reports and annual reports) are submitted to the FDA and other affected parties (e.g., the IRB, other Investigators) in a timely manner (Reference SOPs 202 and 303).
j) Facilitates and coordinates for specific clinical investigations, effective written and oral communications with the National Institutes of Health (NIH) and the FDA, responses to questions, meetings, and reports as necessary.

k) Ensures that clinical investigations are performed according to the Investigational plans and clinical protocols contained in the IND/IDE, and that changes to protocols or participant treatment are reported to appropriate regulatory and institutional authorities (Reference SOPs 301 and 302).
   - Submit to the IRB for approval prior to implementation of the change
   - Submit to the FDA for non-objection prior to the implementation of the change (if applicable)

l) As a Sponsor-Investigator, keeps other investigators informed by means of Investigator Brochures, study and/or annual reports, published literature, observations, and general information concerning the clinical investigation and any significant, new adverse events or risks associated with the investigational product (Reference SOP 303).

m) Selects appropriate (Sub) Investigators on the basis of qualifications, clinical research experience, and knowledge of subject matter, and maintains files on those Investigators involved in the study, including notifying the FDA of their participation (Reference SOP 401 FDA Form 1572).

n) For research conducted under an IND, the Sponsor should ensure that the (Principal) Investigator signs the Investigator Statement for each protocol (aka Protocol Signature Page).

o) For research conducted under an IND or IDE, the Sponsor should ensure that the Investigator understands, signs and adheres to the requirements stated on Form FDA 1572 for IND studies and Investigator Statement for IDE studies.

p) Ensures that other Sub-Investigators and their study staff are adequately prepared to conduct a clinical investigation through site training on the regulations, the protocol and the investigational product. (Reference SOP 401).

q) Ensures regular, timely, effective and well-documented communication among all individuals participating in the conduct of clinical research (Reference SOP 501).

r) Ensures the investigational products are properly labeled and released only to qualified Investigators or designees (such as the local pharmacist), and are distributed, stored and disposed of in a manner that permits full accountability of all investigational product, via appropriate record keeping (Reference SOP PH 75-01).

s) Maintains all required documents and records in an appropriate location and for a period of time specified by regulatory requirements, or study contract, whichever period of time is longer (Reference SOP 503).

t) Assigns someone to monitor the progress of the investigation by performing periodic reviews of participant records and data collected as part of the clinical investigation, including investigational product accountability records, case report forms, other participant records, protocol adherence, adverse event reporting, informed consent, and regulatory documentation (Reference SOP 504).

u) Suspends or terminates an investigation that is determined to present an unreasonable or significant risk to subjects, or for recurring violation of the investigational plan (Reference SOP 506).
v) Protects the rights and well being of study participants and ensures initial and ongoing review by the Memorial Healthcare System Institutional Review Board or other designated IRB.

w) Ensures that each participant signs the current version of the IRB approved informed consent form prior to initiating any study related activities, and continues the process of informing participants about their ongoing participation throughout the duration of the study (Reference SOP 601).

x) Safeguards the scientific, ethical and regulatory validity of the clinical study by requiring strict adherence to participant enrollment criteria, participant identification methods (protection of confidentiality), and biological specimen collection and handling requirements (Reference SOPs 603 and 604).

y) Ensures access to and/or the management of participants' medical care while enrolled, and that adverse events are recorded and, if serious, are promptly investigated and reported to the FDA and other relevant MHS and regulatory authorities (Reference SOP 605).

z) The investigator provides reasonable access to needed medical care during the course of the study, either by the investigator or another qualified individual (when investigator is unavailable and specialized care is needed).

aa) As a sponsor-investigator, maintains a system for recording and managing data and observations from clinical studies, including required safeguards for electronic data collection systems (Reference SOPs 701, 702 and 703).

bb) Employs quality assurance practices that ensure scientific, ethical and regulatory compliance by permitting the independent review and assessment of policies, procedures and records for quality improvement purposes (Reference SOP 801).

c) Cooperates with regulatory authorities (e.g., FDA, OHRP) in their assessment of the clinical research program's compliance with applicable regulations (Reference SOP 802).

### 3.2 General Responsibilities of the Study Team

a) Communicate effectively with participants, other study team members, the IRB, Investigators and the Sponsor.

b) Attend required training activities through their own professional development in relevant content areas.

c) Communicate all adverse events and abnormal laboratory results to the Investigator for an assessment of severity and reports non-serious adverse events or serious adverse events to the IRB, Investigators and Sponsor appropriately.

d) Meet regularly with the Investigator, and other study team members to discuss subject participation and protocol progress.

e) Prepare for and attend Investigator and study start-up meetings.

f) Participate in monitoring visits and audits as appropriate.

g) Make available to Monitors, Auditors, the IRB and regulatory authorities all requested study-related records.

h) Ensure accuracy, completeness, legibility and timeliness of case report forms (CRFs).
3.3 Delegation of Responsibility and Signature Authority

a) The Investigator has the authority to delegate any study-related task or duty to any appropriately qualified member of the study team, who has been properly trained to carry out the designated function, as long as not limited by the protocol's content.

b) The Investigator or his/her designee must identify the individual by name and/or by title, and to which significant study-related functions have been assigned.

c) If a designated individual signs in place of another whose name is typed or printed near the space for signature, the signatory shall sign his or her name followed by the word "for" indicating they are signing for that person.

d) For instances in which the signatory is signing a totally blank space, that person shall simply sign his or her name and provide a date.

e) Start dates on the log should be the date that the person has completed all their required training (CITI, protocol, ICF, received IRB approval (where applicable) and is ready to start their role in the trial as of the date documented. End dates should be the date when the study is officially closed at the site and the IRB has acknowledged the study closure, or the date that the person is no longer working with the institution or OHR.

f) The Principal Investigator should initial (and date where appropriate) showing approval of the personnel listed. The PI should also sign and date at the end of the study.

g) When a new PI replaces an old PI, the old PI should sign and date prior to their departure and the new PI should also sign and date documenting their approval of the personnel listed and their delegated duties. A NTF may be necessary to explain why numerous signatures are on the Log.

3.4 Transfer of Responsibility to Contractors

a) The Investigator has the authority to delegate any study-related task or duty to a qualified contractor (e.g., consulting firm, independent consultant, Contract Research Organization (CRO)) that has been properly trained to carry out the designated function.

b) The Investigator or his/her designee must identify the contracted individual(s) by name and/or by title to which significant study-related functions have been assigned in a properly executed vendor contract.

c) The Investigator will maintain a file documenting the qualifications of such vendors as part of the study file.
4 REFERENCES TO OTHER APPLICABLE SOPS
   • This SOP affects all SOPs.

5 ATTACHMENTS
   A. Signature and Delegation of Responsibility Log
   B. Form FDA 1571
   C. Form FDA 1572

6 APPLICABLE REGULATIONS AND GUIDELINES
   • Responsibilities of Sponsors and Investigators (21 CFR 312 Subpart D)
   • Responsibilities of Sponsors (21 CFR 812 Subpart C)
   • Responsibilities of Investigators (21 CFR 812 Subpart E)
   • The Principles of ICH GCP (ICH E6 sections 2.7 and 2.8)
   • Sponsor (ICH E6 section 5.0)