1 PURPOSE

This procedure describes the activities and processes of the initiation visit and site training for a new clinical study site participating in Investigator-Initiated/Sponsor/Cooperative Group regulated human subject research. It also may be used when a new protocol, an amendment, or a new investigator is added to the study.

2 GENERAL INSTRUCTIONS AND RESPONSIBILITIES

a) The Principal Investigator/Sponsor is responsible for ensuring that all participating Investigators understand and accept the obligations incurred in undertaking participation in a clinical study.

b) The Investigator/Sponsor/designee is responsible for the selection, training, and oversight of Monitors in the use of the investigational product and the conduct of the clinical study.

c) The Investigator/Sponsor/designee is responsible for conducting the initiation visit and training of personnel at the clinical site(s). The trainer will focus on both regulatory requirements and protocol training. The objectives of an initiation visit are:

- Verify that the site's study preparation procedures are completed
- Verify that all regulatory documents are in place
- Verify that investigational product is available so that training can begin
- Review the clinical protocol, case report forms (CRF) and other worksheets
- Review all regulatory requirements
- Provide the plan for study monitoring
- Provide the site with all Sponsor's contact names and telephone numbers
- Confirm the Sponsor's expectations on the conduct of the study
d) The Investigator may consult with the Office of Human Research (OHR) for advice and assistance on regulatory requirements. If the Investigator/Sponsor uses an outside contractor to act as a study monitor, the Investigator/Sponsor will ensure the monitor fulfills the requirements of this SOP.

3 SPECIFIC PROCEDURES

3.1 Preparing for the Initiation Visit

a) When a monitor has not been designated, the Principal Investigator (PI) will be responsible for ensuring that the personnel involved with the conduct of the study have been appropriately trained on the protocol and its requirements.

b) The Investigator, or where applicable, the Monitor/sponsor representative designated to conduct the initiation visit will schedule the visit with the Investigator and the Study Coordinator, making sure that other key personnel who will assist in the conduct of the study are also available, and allowing adequate time for all activities.

c) Prior to the visit, the Investigator or where applicable, the Monitor/sponsor representative should provide the final protocol, informed consent form(s), powerpoint presentation, literature, video, and any other appropriate training materials to the study team for review.

d) Prior to the visit, the Investigator or where applicable, the Monitor/sponsor representative should prepare by reviewing the current protocol and associated CRF and any other relevant documents. They should also confirm with the site: the location of the visit, the necessary personnel who will be present and that no other extenuating circumstances have arisen that would affect attendance.

e) The Investigator or where applicable, the Monitor/sponsor representative should confirm which internal and external regulatory approvals are required for the study, and verify that they have already been received along with the signed contract.

3.2 Internal Site Initiation Visit (SIV)

When a monitor or other designee has not been assigned to the study (e.g. investigator-initiated, cooperative group research studies), it is the responsibility of the Principal Investigator for the site to ensure that his team is appropriately trained. Training should include a gathering of the study’s key personnel to review the following (as necessary):

a. Protocol
b. Eligibility
c. Recruitment/Enrollment
d. Subject/Specimen Management
e. Investigational Product/Pharmacy Requirements
f. Study procedures/Schedule of Events
g. Protocol Compliance
h. Data Management
i. Delegation Log
j. CRF/Worksheet
k. Any outstanding training required by the sponsor
l. Outstanding regulatory items
m. Timelines
n. Reporting Requirements – AE, SAE, PD
The documentation capturing the internal SIV should also include the Name of the Trainer, the date of the SIV, persons who attended, their mode of attendance and which of the above topics were reviewed. The SIV Checklist (Attachment A) will require sign off by persons in attendance and should be filed in the Regulatory Master File upon completion. All persons who were not able to attend the SIV should still provide documentation of training on the protocol for regulatory purposes.

3.3 External Site Initiation Visit (SIV)
When a monitor or other sponsor designee has been appointed for the study, it is their responsibility to schedule a date and time with the Principal Investigator and the site’s research personnel to conduct the initiation visit.

3.3.1 Conducting the Initiation Visit
a) Representatives from all relevant departments participating in the protocol (pharmacy, regulatory, study coordination, recruitment/enrollment, consenting, etc) should be required to attend the initiation visit (in-person, web training or teleconference).

b) Training regarding the areas listed above in 3.2 (as relevant to the study) will be reviewed and discussed.

c) At the meeting, the Monitor or designee will ascertain the Investigator and team's understanding of the required responsibilities through discussions and questions.

d) Key study personnel should be provided sufficient time to discuss questions related to the study and their specific responsibilities during the initiation visit.

e) All persons attending the SIV will be required to sign off on the sponsor provided sign in sheet. The post-visit letter or report, once received from the monitor/designee, should be filed in the Regulatory Master File.

f) All persons who were not able to attend the SIV should still provide documentation of training on the protocol for regulatory purposes.

3.3.2 Monitor Responsibilities
a) The Investigator/Sponsor will ensure that the Monitor or other sponsor designee will review the following items and obligations from the Initiation Visit Checklist with the Investigator and other study personnel:

- Introduction: FDA regulations, other requirements, relevant Sponsor and Investigator standard operating procedures (SOPs)
- Key Personnel Roles Defined: Investigators, Co/Sub-Investigators, other key study personnel, Sponsor, Monitor
- Study Commitment Reviewed: Study contract, study timelines, subject recruitment, subject enrollment, subject and specimen management during the study, protocol compliance
- Documents/Processes Reviewed: Study files, protocol review, CRF, subject case history records, subject coding and randomization, other worksheets,
protocol-related procedures, laboratory procedures, informed consent process, recording adverse events, data management process, inventory accountability records, use of investigational device, investigational dosing, document retention requirements

- Monitoring: Monitoring visit schedule, monitoring procedures/expectations, access to source data and documents, access to CRF and worksheets, Investigator/Monitor meetings
- Investigational Product: Storage and dispensing, required records, inventory disposition
- Reporting Requirements: Data reporting to Sponsor, protocol reporting requirements, reporting unexpected events, reporting adverse events, IRB reporting requirements, FDA reporting requirements

b) The Investigator/Sponsor will ensure that the Monitor will confirm that the Investigator's Regulatory Master File contains the following required items:

- Signed protocol and Investigator Statement
- Signed Investigator contract
- CVs of all participating Investigators
- Form FDA 1572 for IND studies
- IRB approval letter for the protocol
- IRB membership roster
- Final, IRB-stamped, approved informed consent form
- Any other regulatory authority approvals (as determined by the OHR)
- Valid clinical/other laboratory licensure
- Laboratory normal values ranges
- Notice that indicates that the study has been submitted to the FDA
- Investigator Brochure (if appropriate)
- Case report forms
- Investigational product inventory management forms

c) At the initiation visit, the Monitor will instruct and advise relevant site personnel on the pharmacological/technical aspects of the investigational drug/biologic, or device (i.e. review the Investigator Brochure or device specifications and investigational plan).

d) The Monitor will provide the Investigator and other key personnel an opportunity to discuss, and if applicable (for medical devices), provide some hands-on practice with appropriate surrogates or training tools.

e) The Monitor will review instructions for obtaining informed consent, including required signatures and disposition of copies.

f) The Monitor will review instructions for completion of CRFs, including corrections and queries. Draft CRF may be used for training purposes during the initiation visit.
g) The Monitor will review procedures for investigational product accountability, storage, dispensing, reconciliation, discrepancy investigation requirements, and inventory record keeping.

h) The study initiation visit may be held before IRB approval, arrival of investigational product and/or final approved CRF if necessary.

i) Enrollment of the first subject may not occur until the Sponsor has determined that all initiation procedures and regulatory requirements have been completed.

3.4 Documenting the Initial Visit

a) The Investigator/Monitor/designee will document the visit by completing the internal Site Initiation Visit Checklist (Attachment A – internal) or the Site Visit Log (Attachment B – external monitors).

b) The Investigator/Monitor/designee conducting the training will ensure that all persons present are appropriately trained on the requirements of the protocol and the topics listed in section 3.2. A log documenting those in attendance, the date of the training, the name of the trainer and the information covered should be filed in the Regulatory Master File (Attachment A should be completed if one has not been provided by the sponsor).

c) Any supplemental training that takes place at a later date should also be appropriately documented to include what was covered, who attended, the date of the training and the name of the trainer.

d) The Initiation visit discussion and status of required items should be clearly documented.

4 REFERENCES TO OTHER APPLICABLE SOPS

- 501 Communications
- 502 Investigational Product Inventory Management
- 503 Documentation and Records Retention
- 601 Informed Consent
- 602 Subject Recruitment Practices
- 603 Subject Screening and Enrollment
- 604 Specimen Management
- 605 Adverse Event Recognition and Reporting
- 701 Case Report Forms
- 702 Clinical Research Data Management

5 ATTACHMENTS

A. Internal Site Initiation Visit Checklist
B. Site Visit Log
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 Subpart E)
- The Principles of ICH GCP (ICH E6, Section 2.0)
- Compliance with Protocol (ICH E6, Section 4.5)
- Medical Expertise (ICH E6, Section 5.3)
- Trial Management, Data Handling and Record Keeping (ICH E6, Section 5.5)
- Allocation of Responsibilities (ICH E6, Section 5.7)
- Compensation to Subjects and Investigators (ICH E6 Section 5.7)
- Record Access (ICH E6, Section 5.15)
- Multi center Trials (ICH E6, Section 5.23)
- Essential Documents for the Conduct of a Clinical Trial (EHH E6, Section 8.0)