Study Start-Up
SS-204.01

STANDARD OPERATING PROCEDURE FOR
Site Initiation Visit (SIV)

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I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes followed by Georgia CORE when conducting a study initiation visit to:

- Prepare site personnel to implement the protocol according to GCP requirements,
- Review study drug administration and accountability,
- Provide instruction in any specialized procedures such as tissue collection, diagnostic tests and special computer programs,
- Provide direction for CRF completion.

2. SCOPE

This SOP applies to all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics and those which are IND exempt during all investigational phases of development. It describes the steps followed by Georgia CORE from the time a study initiation visit is scheduled until all follow-up activities associated with the visit have been completed. The study initiation visit may be held prior to IRB approval, arrival of investigational product and/or final approval of the CRF if necessary. The study initiation visit should be completed within 30 days of the anticipated IRB approval date and the arrival of the investigational product. Enrollment of the first subject may not occur until all initiation visit procedures and regulatory requirements have been completed.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50	General responsibilities of sponsors
21 CFR 312.52	Transfer of obligations to a contract research organization
21 CFR 312.60	General responsibilities of investigators
21 CFR 312.66	Assurance of IRB review
21 CFR 312.68	Inspection of investigator's records and reports
January 1988	Guidelines for the Monitoring of Clinical Investigations

4. REFERENCES TO OTHER APPLICABLE SOP

SS-201	Assessing Protocol Feasibility
SS-203	Pre-study Site Visits
SM-301	Communication
SM-303	Documentation and Records Retention

5. ATTACHMENT

A. Template Agenda for Site Initiation Visit
B. Initiation Visit Checklist
C. Study Staff Signature Log
D. Site Visit Log

6. RESPONSIBILITY

This SOP applies to members of Georgia CORE involved in managing or participating in the site initiation visit. This includes the following:

- Georgia CORE staff and consultants

7. DEFINITIONS

The following definitions from the International Conference on Harmonisation, Good Clinical Practice: Consolidated Guideline apply to this SOP.

Case Report Form (CRF): A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial.

Clinical trial/study: Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

I**nvestigator**: A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Protocol: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial.

Sponsor: An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial.

Subinvestigator: Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows).

Standard Operating Procedures (SOPs): Detailed, written instructions to achieve uniformity of the performance of a specific function.

8. PROCESS OVERVIEW

The study initiation visit is a meeting arranged and conducted by Georgia CORE and the sponsor, if applicable, to complete the final orientation of the study personnel to the study procedures and GCP requirements. It occurs after the pre-study site visit when all study arrangements have been concluded or are almost complete, and the study is about to start.

A. Preparing for the site initiation visit
B. Participating in the site initiation visit
C. Following-up after the site initiation visit

9. PROCEDURES

A. Preparing for the site initiation meeting

Responsible Staff:	Procedure:
• President	Identify key Georgia CORE staff and consultants likely to be involved in the study under consideration. Assign study to appropriate Georgia CORE staff and consultants. Ensure that all documentation and materials associated with the study are provided to these individuals.
• Research Staff/Consultant	Prepare the meeting agenda (use template in Attachment A as a guideline)

	Develop a Study Manual for the conduct of the study including such documents as:
	• Study Contacts and Responsibility list
	• Communication Plan
	• Georgia CORE website information
	• Instructional materials such as:
	  ○ Case report form (CRF) completion/correction
	  ○ Guidelines for handling adverse events
	  ○ Procedures for handling and storing laboratory specimens
	  ○ Study drug information, including instructions for storing, dispensing and accounting
	• Drug shipment, dispensing and return records
	• Log of study subjects (Master Study Subject Roster)
	• Monitoring log
	
	Review the Site Regulatory Binder to assure that the following documents have been submitted prior to the visit:

	• Signed Form FDA 1572 • Curriculum Vitae (CV) for site Investigator and all sub-investigators – signed and dated • Medical license for site Investigator and all sub-investigators • Financial Disclosure Forms for site Investigator and all sub-investigators • IRB letter of approval • IRB membership roster • IRB approved Informed Consent form • IRB approved advertising, handouts, attachments, etc • Signed copy of the final protocol • Signed copy of Investigator's Drug Brochure (if applicable). • Clinical laboratory certifications and laboratory normal ranges, if applicable • Signed and executed Study Contract Agreement, with budget addendum • Site Delegation log with key site study personnel, with signatures and initials Assure that any materials needed for the meeting (annotated CRFs, sample study medication) are available.

B. Participating in the site initiation visit

• Research Staff/Consultant, with the Sponsor representative	Ascertain the investigator and team's understanding of required responsibilities through discussions and questions (See Attachment A, Template Agenda for Site Initiation Visit, and Attachment B, Initiation Visit Checklist) Provide sufficient time for key study personnel to discuss questions related to the study and their specific responsibilities during the initiation visit Review the following key items and obligations from the Initiation Visit Checklist with the investigator and other key personnel: • Introduction: FDA regulations, other requirements, relevant investigator standard operating procedures • Key personnel roles defined: investigator, sub-investigators, other site key research personnel, 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, inclusion/exclusion criteria, 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 drug 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, protocol reporting, reporting unexpected events, reporting adverse events, IRB reporting requirements, FDA reporting requirements

Confirm that the investigator's study file contains the following required items and indicate on the Initiation Visit Checklist:

- Signed protocol and Investigator Statement
- Signed and executed Investigator contract
- CVs and licenses of key site study staff
- Financial Disclosure forms
- Form FDA 1572 for IND studies
- IRB approval letter for the protocol
- IRB membership roster
- Final, IRB-stamped, approved informed consent form
- Institutional and/or other regulatory authority approvals
- Valid clinical/other laboratory licensure
- Laboratory normal value ranges
- Notice that indicates the study has been submitted to the FDA
- Investigator Brochure, if appropriate
- Case report forms
- Investigational product inventory management forms

Review with all site personnel the use of relevant logs, e.g.

	Attachment C, Study Staff Signature Log and Attachment D, Site Visit Log and the Investigators' Exchange and GeorgiaCancerTrials.org web sites. 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) Provide the investigator and other key study staff an opportunity to discuss, and if applicable (for medical devices), provide some hands-on practice with appropriate surrogates or training tools Review procedures for obtaining informed consent, including required signatures and disposition of copies Review instructions for completion of CRFs, including corrections and queries. Draft CRF may be used for training purposes during the initiation visit Review procedures for investigational product accountability, storage, dispensing, reconciliation, discrepancy investigation requirements, and inventory record keeping

C. Following up after the site initiation meeting

* Research Staff/Consultant	Document the visit by signing the Site Visit Log. Ensure the initiation visit discussion and status of required items is documented on the Initiation Visit Checklist. Ensure the Initiation Visit Checklist is filed in the appropriate section of the Investigator's Regulatory Master File.

10. History of Changes

Version Number	Section Number	Modification	Approval Date
204.00	All	Original Version	
204.01	9 B	Addition of regulatory paperwork required (bullets 4, 10 and 13)	09 March 2012
204.01	All	No changes necessary	01 July 2014
204.01	All	No changes necessary	21 March 2017

Attachment A

TEMPLATE AGENDA FOR SITE INITIATION VISIT		
10 minutes	Welcome and introductions	Georgia CORE, Investigator, Key research staff, Sponsor personnel, if applicable
1-3 hours	Review key items and obligations from the Initiation Visit Checklist	Georgia CORE, Investigator, key research staff, Sponsor personnel, if applicable
1 hour	Review the Investigator's study file and indicate findings on the Initiation Visit Checklist	Georgia CORE, Sponsor personnel, if applicable
1 hour	Review • use of relevant logs • pharmacological and technical aspects of the investigational product • procedures for informed consent • instructions for completing CRFs • procedures for investigational product management	Georgia CORE, Investigator, Key research staff, Sponsor personnel, if applicable
1 hour	Discussion time, including questions and answers	Georgia CORE, Investigator, Key research staff, Sponsor personnel, if applicable
5 minutes	Summary and Next Steps	Georgia CORE and Investigator

Attachment B

SITE INITIATION VISIT CHECKLIST

Date:

Site: _____ **Sponsor:** _____

_____ _____

_____ _____

Investigator: _____ Phone: _____

Sub-Investigator: _____ Phone: _____

Sub-Investigator: _____ Phone: _____

Key Study Contact: _____ Phone: _____

Research Coordinator: _____ Phone: _____
(if other than Key Study Contact)

Other study personnel:

Name: _____ Title: _____

Name: _____ Title: _____

Name: _____ Title: _____

A. Confirm information provided to the site	Yes	No	N/A
1. Confidentiality agreement signed by Investigator	☐	☐	☐
2. Protocol received and reviewed by Investigator	☐	☐	
3. Understanding of relevant scientific background information	☐	☐	
4. Study timeline, initiation, subject accrual rate and completion	☐	☐	
5. Roles and responsibilities of all key Investigator personnel	☐	☐	
6. Monitoring schedule, types of visits, agenda and attendees	☐	☐	
7. Investigational product inventory management	☐	☐	☐
8. Reporting and record-keeping requirements	☐	☐	

B. Clinical study regulatory requirements	Discussed?		
1. *Obligations of Investigator and key study personnel*	Yes	No	
• Conduct study according to written protocol, federal regulations, IRB and other applicable regulatory requirements	☐	☐	
• Document all unanticipated events and immediately contact study Monitor for follow-up instructions	☐	☐	
• Accurately report all data and observations of anticipated and unanticipated adverse events/device malfunctions	☐	☐	
• Observe Good Clinical Practice (GCP), and if appropriate, Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP)	☐	☐	
2. Human subject safety and confidentiality	Yes	No	N/A
• Conduct informed consent process according to regulatory and IRB requirements	☐	☐	
• Participant identifiers will be properly masked and samples will be coded per protocol requirements	☐	☐	☐
• Storage of participant records secure, protects their confidentiality	☐	☐	
3. Reporting of study results	Yes	No	N/A
• Results of investigational device use cannot be used for patient diagnosis or management	☐	☐	☐
• Stipulations for scientific publications and presentations at professional meetings	☐	☐	☐

C. Study management and record-keeping requirements	Discussed?		
1. Data collection, verification and transmission procedures	Yes	No	N/A
• Timely completion of case report forms (CRF)	☐	☐	☐
• CRF review and verification for accuracy	☐	☐	☐
2. *Contents of Investigator's study file*	Yes	No	
• Investigator's records, e.g., signed study contract, names of site personnel participating in the study and their qualifications	☐	☐	
• Protocol, CRF and amendments, source documents/participant case histories	☐	☐	
• Communication and site visit logs, product inventory logs, copies of relevant correspondence (Investigator, IRB, FDA)	☐	☐	
3. Investigational product inventory requirements	Yes	No	N/A
• Research pharmacist available	☐	☐	☐
• Receipt log of all investigational product	☐	☐	☐
• Accurate and current records of investigational product use	☐	☐	☐
• Verification of investigational product accountability	☐	☐	☐
4. Record retention and accessibility	Yes	No	N/A
• Administrative and subject records maintained for at least two years after the study is closed out and/or (as applicable) FDA clears/approves the product	☐	☐	
• Requirement for review of records by institutional Monitors, Auditor	☐	☐	
• Requirement for review of records by government officials (FDA, Agent of NIH/HHS, state)	☐	☐	☐

D. Adverse event/device malfunction reporting requirements	Discussed?		
1. Contact Monitor, or if applicable Investigator, by telephone to report serious, life-threatening or fatal unanticipated adverse events immediately	Yes ☐	No ☐	
2. File written reports as stipulated by Investigator and IRB	Yes	No	N/A
• Unanticipated serious, life-threatening or fatal adverse event to Investigator and IRB	☐	☐	
• Unanticipated, non-serious adverse events in required progress reports to Investigator and IRB	☐	☐	
• Anticipated serious adverse events to Investigator	☐	☐	
• Device malfunctions immediately to Investigator	☐	☐	☐
3. Other required reports	Yes	No	N/A
• Periodic participant accrual status reports to Investigator	☐	☐	
• Final study report to Investigator and IRB	☐	☐	☐
• Required progress reports to IRB	☐	☐	

E. Reviewed protocol with Investigator and key study personnel	Yes	No	N/A
1. Purpose of the study	☐	☐	
2. Inclusion/exclusion criteria	☐	☐	
3. Dosing regimen for drug studies	☐	☐	☐
4. Specimen collection, storage and processing procedures	☐	☐	☐
5. Required clinical information needed for study	☐	☐	
6. Performance evaluation and interpretation of results	☐	☐	☐
7. Data collection and completion of case report forms	☐	☐	☐
8. Criteria for study completion or termination	☐	☐	
9. Documenting protocol violations (deviations from the protocol)	☐	☐	☐

F. Other Monitor Observations

Describe general impressions from the site initiation visit.

G Discuss Significant Concerns

H. Summary and Conclusion

Monitor's Name (print)	Signature	Date
Investigator's Name (print)	Signature	Date

Attachment C

STUDY STAFF SIGNATURE LOG

Print Name	Signature	Initials

Attachment D

SITE VISIT LOG

Investigator:_____ **Site:** _____
Protocol Number/Title: _____

_____

Date of Visit	Name of Monitor	Type of Visit*	Monitor Signature	Staff Initials

Type of Visit*	Code	Definition of Visit Type
Initiation	I	Initial study training, review of regulatory requirements.
Scheduled	S	Periodic routine monitoring visits.
Unscheduled	U	Monitoring visit to verify protocol non-compliance.
Close-out	C	Final visit to close out study for any reason.
Other	O	