General Administration
GA – 102.01

STANDARD OPERATING PROCEDURE FOR
Sponsor Responsibility and Delegation of Responsibility

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(Signature and Date)

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1. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) defines Georgia CORE's responsibilities in the conduct of research studies.

2. SCOPE

This SOP defines the responsibilities of Georgia CORE as the sponsor for conducting Investigator-initiated research studies. This SOP applies to all studies subject to investigational new drug (IND) regulations for drugs and biologics or those eligible for investigational new drug (IND) exemption during all investigational phases of development. Investigator driven studies are those studies which are initiated by an Investigator who is the holder of the IND or IDE or whose study has met the criteria for an IND exempt study.

Georgia CORE will follow this SOP for those sponsor responsibilities delegated by a Pharmaceutical Sponsor when Georgia CORE serves as a site management organization (SMO) for an industry-initiated study.

The SOP identifies administrative accountability as well as general responsibilities of Georgia CORE for fulfilling regulatory and clinical requirements. The SOP also identifies Georgia CORE's expectations of administrative accountability as well as general responsibilities of the Investigator and Subinvestigators and other site research team members for fulfilling regulatory and clinical requirements.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50	General responsibilities of sponsors
21 CFR 312.53	Selecting Investigators and monitors
21 CFR 312.60	General responsibilities of Investigators
21 CFR 46	46DHHS Part 46 Protection of Human Subjects
21 CFR 312.61	Control of the investigational drug
21 CFR 312.62	Investigator recordkeeping and record retention
21 CFR 312.64	Investigator reports
21 CFR 312.66	Assurance of IRB review
21 CFR 312.68	Inspection of Investigator's records and reports
21 CFR 312.69	Handling of controlled substances
21 CFR 54	Financial Disclosure by Clinical Investigators
January 1988	Guidelines for the Monitoring of Clinical Investigations
October 2009	Guidance for Industry Investigator Responsibilities--- Protecting the Rights, Safety, and Welfare of Study Subjects
January 2004	Guidance for Industry IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer, Revision 1

FDA Information Sheets October 1998	Frequently Asked Questions, Continuing Review After Study Approval, Recruiting Study Subjects, Payment to Research Subjects, Screening Tests Prior to Study Enrollment, A Guide to Informed Consent, Sponsor-Investigator-IRB Interrelationship
May 1997	International Conference on Harmonisation; Good Clinical Practice: Consolidated Guideline

4. REFERENCES TO OTHER APPLICABLE SOPs

All SOPs are applicable to this SOP.

5. ATTACHMENTS

A. Study Team Responsibilities
B. Form FDA 1572
C. Form FDA 3454
D. Form FDA 3455
E. Delegation of Responsibility Form

6. RESPONSIBILITY

This SOP applies to Georgia CORE leadership, staff members and consultants involved in trials. This includes the following:

- President and CEO
- Chief Medical Officer
- 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.

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.

Investigator: 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.

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).

8. PROCESS OVERVIEW

A. Fulfilling Regulatory Obligations

B. Delegation of Responsibility

C. Transfer of Responsibility to Contractors

9. PROCEDURES

A. Fulfilling Regulatory Obligations

• President and CEO	Ensure that an IND/IDE is obtained by the Investigator or that the study is deemed an exempt study. Manage the business aspects of studies, including developing and negotiating study budgets and contracts. Review the Investigator responsibilities with the Investigator
• Staff and Consultants	Follow standard operating procedures (SOP's) to ensure that the conduct of human subject research proceeds in compliance with GCP Guidelines and all applicable regulations and organizational requirements are met. Select qualified Investigators/Subinvestigators, on the basis of qualifications, research experience, and knowledge of subject matter, and maintain files on those Investigators/Subinvestigators involved in the study. Notify the FDA of the Investigator/Subinvestigator involvement for studies conducted under an IND/IDE. (Reference SOP 202.00 Investigator Selection and SOP SS 203 Pre-study Site Visit) Ensure that the Investigator, Subinvestigators, and study teams are aware of their respective responsibilities for the study. (Attachment A: Study Team Responsibilities) Ensure that the Investigators signs the Investigator Statement for each protocol and signs and adheres to the requirements stated on Form FDA 1572 (Attachment B: Form FDA 1572) Ensure that financial and professional conflicts of interest

are recognized, reported to appropriate authorities, and any applicable management plans are followed. (Attachment C and D: Financial Certification and Disclosure Forms)

Ensure that responsibilities and activities in the conduct of 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 training and experience to carry out those responsibilities and activities, with appropriate documentation of that delegation. (Attachment E: Delegation of Responsibility Form)

Ensure that critical documents are developed, reviewed, approved, and modified in a controlled and accountable manner. (Reference SOP GA 101, Standard Operating Procedure Preparation and Maintenance and SOP GA 104, Document Development and Change Control).

Establish criteria for selecting qualified outside contractors to conduct study-related activities when necessary and appropriate, and document those selection criteria and delegated responsibilities.

Provide Investigators and Subinvestigators with the information they need to conduct the investigation properly.

Working with the Investigator, keep Subinvestigators informed by means of Investigator Brochures, published literature, observations, and general information concerning the study and any significant, new adverse events or risks associated with the investigational product. (Reference SOP 301 Communication)

Ensure regulatory documents are completed and submitted as appropriate during study initiation, study conduct and study closure. (Reference SOP SM 303 Documentation and Records Retention)

Ensure proper monitoring of the study. (Reference SOPs SS 204 Site Initiation Visit, SM 304 Routine Monitoring Visits, SM 305 Closeout Visits)

Monitor the progress of the investigation by performing periodic reviews of subject records and data collected as part of the study, including investigational product accountability records, case report forms, other subject records, protocol adherence, adverse event reporting, informed consent(s), and regulatory documentation.

Communicate with the Investigator and/or Subinvestigator and IRB any information contained in a monitoring report, or summary report, of Georgia CORE's assessment that could affect the rights or welfare of the study subjects or their willingness to continue in the study. Examples

include, but are not limited to: major protocol deviations, failure to obtain informed consent, misuse of investigational drugs or devices, or fraud. (Reference SOP SM 302 Interactions with the IRB)

Ensure that the FDA (for IND/IDE studies), the reviewing IRBs and all participating Investigators receive all relevant reports (e.g. study reports, adverse event reports, safety reports, and continuing review reports) in a timely manner.

Ensure that studies are performed according to the protocol, and that changes to the protocol or subject treatment are reported to appropriate regulatory and institutional authorities.

- Submit to the IRB for approval prior to implementation of the study and/or the change
- Submit to the FDA for non-objection prior to the implementation of the change (if applicable)

Review subject recruitment strategies for appropriateness and track study enrollment.

Ensure that Investigators, Subinvestigators and their study staff are adequately prepared to conduct a study through site training on the regulations, the protocol and the investigational product.

Ensure regular, timely, effective and well-documented communication among all individuals participating in the conduct of the study. (Reference SOP SM 301 Communication)

Ensure the investigational products are manufactured under appropriate controls, are properly labeled and released only to qualified Subinvestigators, and are distributed, stored and disposed of in a manner that permits full accountability of all investigational product, via appropriate record keeping. (Reference SOP 307 Investigational Product Management)

Maintain all required documents and records in the appropriate location and for a period of time specified by regulatory requirements.

Terminate a study that is determined to present an unreasonable or significant risk to subjects, or for recurring violation of the protocol.

Protect the rights and well being of study subjects and ensure initial and ongoing review by an IRB. (Reference SOP PP 501 Safeguarding Protected Health Information)

Safeguard the scientific, ethical, and regulatory validity of the study by requiring strict adherence to subject

	enrollment criteria, subject identification methods (protection of confidentiality), and biological specimen collection and handling requirements. (Reference SOP SM 308 Specimen Management) Ensure the management of subjects' medical care while enrolled and that adverse events are recorded and, if serious, are promptly investigated and reported appropriately. (Reference SOP SM 306 Adverse Event Reporting) Working with the Investigator, maintain a system for recording and managing data and observations from studies, including required safeguards for electronic data collection systems. (Reference SOP DM 401 Data Management) Employ 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. Cooperate with regulatory authorities (e.g., FDA, OHR) in their assessment of the study's compliance with applicable regulations. (Reference SOP QA 601 Audit by Third Parties) Ensure appropriate registration of the study.

B. Delegation of Responsibility

• President and CEO • Contracts and Regulatory Administrator • Chief Medical Officer • Georgia CORE staff and consultants	Sponsor studies according to FDA regulations and guidelines and Georgia CORE's SOPs. Ensure Georgia CORE staff are properly trained to carry out responsibilities for each study. Ensure the safety and welfare of study subjects by being knowledgeable about ongoing study protocols and investigational articles.

C. Transfer of Responsibilities to Contractors

• President and CEO	Transfer responsibility for any or all of the obligations that may be made to a qualified contractor or to the Investigator with any such transfer described in writing. If not all obligations are transferred, the writing is required to describe each of the obligations being assumed by the contractor or by the Investigator.
• Contracts and Regulatory Administrator	Maintain a file documenting the transferred obligations and the qualifications of such contractors or Investigator as part of the study file.

10. History of Changes

Version Number	Section Number	Modification	Approval Date
102.00	All	Original Version	
102.01	Attachment A	Additions to Nurse/coordinator responsibilities	09 March 2012
102.01	Attachment B	Updated website information	09 March 2012

Attachment A

STUDY TEAM RESPONSIBILITIES

General responsibilities of the study team

• PI • Subinvestigator • Research nurse/coordinator • Data manager • Research assistant • Study pharmacist • Support staff	Conduct studies according to FDA regulations and guidelines and SOPs of the site Communicate effectively with subjects, other study team members, the IRB, the Investigator and Georgia CORE. Ensure the safety and welfare of study subjects by being knowledgeable about ongoing study protocols and investigational articles. Communicate all adverse events and abnormal laboratory results to the Subinvestigator for an assessment of severity and report adverse events to the IRB, the Investigator and Georgia CORE appropriately. (Reference SM 306 Adverse Event Reporting) Meet regularly as a team to discuss subject participation and protocol progress. Prepare for and attend Investigator and start-up meetings. Participate in monitoring visits and audits as appropriate. Make available to Monitors, Auditors, the IRB and regulatory authorities all requested study-related records. Ensure accuracy, completeness, legibility and timeliness of case report forms (CRFs). Ensure that CRFs accurately reflect source documents, explain any discrepancies between source documents and CRFs. Comply with written SOPs to document changes and/or corrections to data and/or CRFs. Ensure documentation of study-related procedures, processes and events. Maintain study documents and files as required by the regulations for the appropriate time frame and under secure conditions. Comply with federal regulations governing disclosure of personal, professional or financial interests in a research study that may impact upon its conduct, evaluation or outcome. Support required training activities through each team members' own professional development in relevant content areas.

Individual responsibilities within the research team
Team member titles may be different at each site
Additional responsibilities may be assigned to team members

• Investigator	Write and submit Research Concept Proposal (RCP) form and submit to Georgia CORE. Participate in RCP review process. Upon approval to proceed by Georgia CORE, write and submit protocol. (Reference SOP SS-201 Assessing Protocol Feasibility) Submit protocol to FDA for IND/IDE or submit acceptable rationale for IND/IDE exemption to Georgia CORE and the appropriate IRB. Provide FDA contact and IND number and initial approval letter from the FDA for the study. (if applicable) Complete all required IND/IDE regulatory paperwork and submit to the FDA, and appropriate IRB, and Georgia CORE. Write plan for investigational product security, screening/enrollment/follow-up and data collection. Write or supervise writing of eCRF/CRFs and related documents. Review all AEs, SAEs, deviations, and endpoints and determine causality. Determine if protocol and/or informed consent should be modified based on findings and follow-up as appropriate. (Reference SOP SM 306 Adverse Event Reporting) Review and sign monitored and completed eCRF/CRF Review periodic Investigator trial report, which includes when applicable • AE, SAE, deviation, outcome list (affirm or reassign causality) • IND safety report list • Interim IND safety reports • Trial newsletters • Significant pharmaceutical and Georgia CORE correspondence • Study monitor correspondence, e.g., pre-visit report, visit summary report, site response • Interim IRB correspondence

	Ensure medical expertise is available for all study-related medical queries or patient care. Ensure appropriate overall study management, data handling, and record keeping Ensure that study records are maintained for the appropriate time. Ensure appropriate manufacture, packaging, labeling/coding and distribution to study sites of all investigational products. Complete study report.
• Investigator • Subinvestigator	Under FDA regulations and guidance, Investigators and Subinvestigators are responsible for the conduct of the study and for leading the team of individuals conducting the study. Their responsibilities include the following: Sign Form FDA 1572 to acknowledge responsibilities as defined by the regulations (Attachment B, Form FDA 1572). Provides Investigator qualifications and agreements. Provide Georgia CORE with required information that either: Attests to the absence of financial interests or arrangements as described in the regulations (CFR 54.4) and reported on Form FDA 3454 that is completed by the sponsor), (Attachment C, Form FDA 3454 link) or Provides Georgia CORE with a complete and accurate disclosing of financial interests and arrangements as described in the regulations (CFR 54.4) and reported on Form FDA 3455 that is completed by Georgia CORE. (Attachment D, Form FDA 3455 link) Participate as appropriate in the hiring and training of individuals recruited as members of the research team. Assign trained research nurse/coordinator(s) to manage each study planned or ongoing at the site. Determine whether adequate resources are available to conduct the study. While retaining knowledge of and overall authority for the conduct of studies at the site, supervise members of the research team qualified by their education and training (and state and local laws) to accept these responsibilities for study-related activities not directly performed by the Investigator or Subinvestigator. Document the delegation of responsibilities (Attachment E,

	Delegation of Responsibility Form). Ensure the safety and welfare of study subjects by being knowledgeable about ongoing study protocols and investigational articles. Ensure that specific Georgia CORE requirements of the Investigator or Subinvestigator are fulfilled as requested. Meet with Georgia CORE representatives as appropriate to discuss planned and ongoing studies. Meet with auditors (internal, Georgia CORE, FDA as applicable) at the conclusion of their audits to review findings. Manage the medical care of the subjects. Ensure informed consent of each subject is obtained. Ensure the study is conducted according to the protocol. Personally conduct or supervise the study. Prepare and maintain adequate, current, and complete case histories or records. Ensure the validity of the data reported. Ensure documentation of study-related procedure, processes, and events. Ensure privacy and security of the research data. Retain records for the required period of time. Furnish the required reports to Georgia CORE, including reports of adverse events and study completion. Provide timely reports to the IRB (or Georgia CORE if using a central IRB), including reports of changes in the research activity needed to avoid immediate hazards to study subjects, unanticipated problems involving risks to study subjects or others, including adverse events to the extent required by the IRB. Ensure that changes are not implemented without prospective IRB approval, unless required to eliminate immediate hazard to the study subjects. Comply with the requirements of the Controlled Substance Act. Comply with all FDA test article requirements. Adequately maintain control of test articles, including appropriate tracking documentation. Supervise the use, storage and disposition of the investigational product. Direct site operations in relation to the management of the

	study. Maintain professional and technical knowledge.
• Research Nurse/Coordinator	Manage all aspects of conducting the study. Maintain an in-depth knowledge of protocol requirements and good clinical practices as set forth by federal regulations and guidelines and site SOPs. Serve as liaison between the Investigator/Subinvestigator, primary care providers, the IRB and Georgia CORE. Develop organizational aids and checklists to facilitate patient recruitment and enrollment as well as the collection of complete and accurate study data. Enroll subjects in studies and manage their participation according to ethical, regulatory, and protocol-specific requirements. Maintain the regulatory and study files for each research project. Collect study data and complete Data Collection Worksheet/e-CRF/CRF, data query resolution and corrections. Collect and report AE's, SAE's, Deviations and Endpoints within the time period set forth by the site's ethic review boards and protocol requirements. Collect, process, and ship lab samples according to protocol reguirements and local, state and federal IATA requirements Participate in quality assurance activities (monitoring visits, internal audits, sponsor audits, FDA audits).
• Data Manager	Enter data on to case report forms (CRFs), and/or key data using remote data entry. Collect all source documentation and worksheets prepared by research team members and transcribe data onto the appropriate collection tool for submission.
• Research Assistant	Assist the research nurse or coordinator in conducting the study. Collect, process, store, and handle specimens, schedule study patients for follow-up. Collect, record and file data.

Attachment B

FORM FDA 1572

STATEMENT OF INVESTIGATOR

To retrieve (PDF) format of the above forms go to web site:

http://ctep.cancer.gov/forms/docs/FDA_Form_1572_Final.pdf

Download this form, or Xerox a copy of the form provided as an attachment in the SOP printed document.

Attachment C

FORM FDA 3454

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

To retrieve (PDF) format of the above forms go to web site:

http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048304.pdf

Download this form, or Xerox a copy of the form provided as an attachment in the SOP printed document.

Attachment D

FORM FDA 3455

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

To retrieve (PDF) format of the above forms go to web site:

http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm048310.pdf

Download this form, or xerox a copy of the form provided as an attachment in the SOP printed document.

Attachment E

DELEGATION of RESPONSIBILITY FORM

I, _____
_____MD, located at _____
_____am Principal Investigator for Protocol #_____
_____ entitled _____
_____

I have ensured that the individuals listed below are properly qualified and have received appropriate training. Based upon this, I have delegated the following responsibilities to the individuals named below, and assert that these duties will be performed under my direct supervision:

RESPONSIBILITY	***PERSONNEL***	***DATE***
Administration		
Contract negotiations		
Fiscal management		
Strategic planning		
Patient database		
Performance tracking		
Quality assurance		
Study Management		
IRB submissions & communications		
Patient recruitment activities		
Sponsor, CRO contact		
Regulatory files creation and maintenance		
Data management/CRF completion		
Adverse event reports		
Organizational tools		
Office staff training		
Storing, dispensing, accounting for study drug		
Overall study drug accountability		
Storing study documents		
Subject Management		
Screening subjects for eligibility		
Obtaining informed consent		
Subject education		
Monitoring patient compliance		
Subject enrollment and follow-up		
Clinical assessments		
Adverse event determination		
Source documentation		
Appointment scheduling		

_____ _____/_____/_____

Signature Date