Quality Assurance
QA – 601.01

STANDARD OPERATING PROCEDURE FOR FDA or Pharmaceutical Sponsored Audits

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1. INTRODUCTION

This standard operating procedure (SOP) describes the processes followed by Georgia CORE for a third party audit (e.g. sponsor/CRO or FDA) to assess compliance with regulatory requirements/guidelines and SOPs related to clinical research.

2. SCOPE

This SOP describes the steps followed by Georgia CORE from the time the audit or inspection is scheduled until all follow-up activities associated with the audit or inspection has been completed. For the purposes of this document the term 'audit' addresses both audits and FDA inspections and the term 'auditor' includes both auditors and FDA inspectors.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.58	Inspection of sponsor's records and reports
21 CFR 312.60	General responsibilities of investigators
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
December 2008	FDA Compliance Program Guidance Manual For FDA Staff, 7348: 811 Bioresearch Monitoring: Clinical Investigators
June 2010	FDA Information Sheets: Clinical Investigator Inspections
May 9, 1997	International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline
January 1988	FDA Guidelines for the Monitoring of Clinical Investigations

4. REFERENCES TO OTHER APPLICABLE SOPS

All SOPs are applicable to this SOP

5. ATTACHMENTS

A. Preparing for an Audit Checklist

6. Responsibility

This SOP applies to Georgia CORE leadership, staff members and consultants involved in arranging, managing, or participating in a third party audit and/or monitoring a site that is being audited by a third party. 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 Harmonization, Good Clinical Practice: Consolidated Guideline apply to this SOP.

Audit: A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).

Audit Trail: Documentation that allows reconstruction of the course of events.

Compliance: Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements.

Direct Access: Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsors, monitors, and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information.

Documentation: All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

Essential Documents: Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Quality Assurance (QA): All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

Quality Control (QC): The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

Source Documents: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial).

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

8. PROCESS OVERVIEW

A. Preparing for the audit
B. During the audit
C. Following up after the audit

9. PROCEDURES

A. Preparing for the audit

• President and CEO or Designee	Notify the sponsor and/or Investigator who initiated the study, if applicable, when notified of a third party audit as soon as possible Work with the auditor to develop a proposed schedule (estimated number of days, times) for the audit (to the extent possible) and ensure that all key personnel will be available before confirming a date Ensure that records of staff qualifications and training are available for review by the auditor
• Georgia CORE staff and Consultants	Review Presentation: Preparing for an FDA Clinical Investigator Inspections at www.fda.gov/Training/CDRHLearn/ucm180878.htm if this is a FDA inspection
• Contracts and Regulatory Administrator	Ensure that all study documentation, including the regulatory binder, study templates, study communication records and electronic records maintained by Georgia CORE for the study identified as the focus of the audit are accurate, complete and available for review by the auditor (Attachment A, Preparing for an Audit Checklist) Ensure that Standard Operating Procedures are available
• President and CEO or Designee	Review with Georgia CORE staff who will be involved in the audit the following guidelines: • Documents that the FDA may not inspect, absent voluntary production by Georgia CORE, include but are not limited to: o Financial data o Personnel data (other than that needed to establish the qualifications of technical and professional personnel performing functions involved in the study)

	○ Internal QA audit records • Use of still or video cameras, or voice recording apparatus, on Georgia CORE's premises by the auditor must be agreed to by the President and CEO. If the decision is made to allow the use of the equipment, the President and CEO will determine that Georgia CORE's rights and privileges will not be waived, that Georgia CORE will be given equal opportunity to use the same equipment, and appropriate measures have been taken to ensure the protection of proprietary or confidential information of Georgia CORE and/or its employees and research sites and research subjects • The auditor may request to view electronic data files on a computer and to make copies of electronic data files on a memory device to be provided to him/her as part of the audit document collection process. This request must be reviewed and agreed to by the President and CEO of Georgia CORE • The President and CEO or Designee must approve all auditor requests for copies of documents and records and review the copies of documents and records before handing them to the auditor in order to be satisfied that appropriate measures have been taken to ensure the protection of proprietary or confidential information contained in those documents and records • The President and CEO must be consulted if the auditor requests that an affidavit or any other document be signed, initialed or otherwise ratified
• President and CEO or Designee	Designate an individual to take notes of activities and discussions during the audit Designate an individual to make copies and obtain documents and records as requested Identify adequate space for the auditor to use to review documents and records

• Designee	Ensure that the Investigator, Subinvestigator and site staff are instructed to notify the Designee if they are notified by a third party that their site will be audited Request that the Investigator, Subinvestigator and key site staff review Presentation: Preparing for an FDA Clinical Investigator Inspections at www.fda.gov/Training/CDRHLearn/ucm180878.htm if this is a FDA inspection Review the following with the site staff prior to a scheduled audit to ensure that: • all key study personnel will be available for the audit before the audit date is confirmed • all study documentation, including informed consent forms, source documents, electronic records, CRFs, and the regulatory binder for the study identified as the focus of the audit are accurate, complete and available for review by the auditor (Attachment A, Preparing for an Audit Checklist) • Standard Operating Procedures are available • study drug dispensing records should be accurate, complete and available for review. If there were any instances in which emergency breaking of the blind was required, that documentation is available • study drug accountability records are accurate, complete and available for review • records of staff qualifications and training are available for review by the auditor.

B. During the audit

• President and CEO or Designee	Meet with the auditor. Request to see identification, and if this is an FDA audit, request Form FDA 482, Notice of Inspection and ascertain the purpose of the inspection Review the policies and guidelines for the conduct of the audit with the auditor Provide orientation and access to the study records and files Ensure that the auditor is not left unattended and arrange for appropriate staff to be available to answer questions, retrieve documents, and facilitate completion of the audit Document all relevant discussion and requests Provide copies of requested study-related documents; ensuring a second copy of each document is made and kept

	in Georgia CORE's audit file Review the copies to redact any proprietary or confidential information before the copy is given to the auditor Ensure that questions posed by the auditor are answered by appropriate personnel and request additional time to respond if necessary Request an opportunity to immediately correct objectionable observations Ensure that the auditor does not remove an original document or record from Georgia CORE's premises, nor makes any copies him/herself nor makes any marks on original documents and records Request that a summary of audit findings be provided at the end of each day Meet with all relevant key personnel to discuss and summarize the day's events after the auditor has departed

C. Following up after the audit

• President and CEO or Designee	Participate in the exit interview with the auditor; include all relevant personnel at the meeting. If this was an FDA audit, a signed Form FDA 483 (Inspectional Observations for significant deviations from the regulations) should be given to the President and CEO or Designee by the FDA auditor if the Form FDA 483 is to be issued If observations can be corrected before the end of the audit, attempt to do so and the auditor may annotate the report or Form FDA 483 to document that the observation was corrected or a corrective process was put in place. Request a copy of the annotated or corrected report or Form FDA 483, if applicable Ask the auditor to clarify any items and provide as much detail as appropriate for items that need such clarification Express explanations or disagreements about any items or issues clearly, assertively and respectfully
• President and CEO or Designee	Respond to the Form FDA 483 and then the audit report as soon as possible after its receipt, within any required deadlines. Reply to each item in the report, including: • An evaluation of the extent of the problem • Assessment of the root cause of the problem • Any corrective actions: what was or will be corrected, when was it or will it be completed, is the problem systemic

	• Preventive actions to prevent recurrence of the problem in future studies • Time frame for training • Supporting documentation Send a written request to the FDA for a copy of the Establishment Inspection Report (EIR) 30 days after a FDA inspection Contact the FDA office and request the status of the letter if a letter from the FDA officially classifying the Inspection (No Action Indicated, Voluntary Action Indicated, Official Action Indicated) is not received within 45 days of the inspection Retain copies of any audit documents in the appropriate file
• Designee	Participate in the exit interview with the auditor, the Investigator and/or Subinvestigator and relevant site staff for audits of network sites when the audited study is sponsored by Georgia CORE or Georgia CORE is serving as the Site Management Organization (SMO) Meet with the Investigator and/or Subinvestigator and relevant site staff after the exit interview with the auditor to discuss required next steps Request that the site send draft responses to audit reports and/or Form FDA 483 to the Designee prior to formal submission to the auditor or FDA. Review draft and provide feedback to the appropriate site staff member within one business day. Notify President and CEO and Medical Director of all audit findings and follow up, as applicable Confer with the President and CEO and Medical Director about reporting audit results to other relevant regulatory authorities or funding sponsors

10. History of Changes

Version Number	Section Number	Modification	Approval Date
601.00	All	Original Version	
601.01	Section 3	Addition of June 2010 Federal Regulations for Clinical Investigator Inspections	09 March 2012
601.01	All	No changes necessary	01 June 2014
601.01	All	Modification of Title	01 March 2017

Attachment A

PREPARING FOR AN AUDIT CHECKLIST

I. ORGANIZATION		Completed	N/A	COMMENTS
	Industry Sponsor (if an FDA audit)			
	IRB			
Notify all parties involved with the clinical study	Investigator, Subinvestigators			
	Pharmacy			
	Laboratories			
	Medical records			
	Administration			
	Legal counsel			
	Reserve work space for the auditor			
General overview of the study	Prepare a general overview of the study			
	List all personnel and responsibilities delegated (study delegation sheet)			
List of subjects	List all subjects enrolled including name, address, and/or phone number, date enrolled and completed, medical record number (to be kept as a reference for site research staff)			
	List all subjects screened			
Standard Operating Procedures (SOPs)	SOPs for conduct of study			

2. FILES MANAGEMENT		YES	N/A	COMMENTS
Organize all regulatory files by general heading arranged in chronological order	Protocol (all versions)			
	Investigator's Brochure (all versions)			
	Protocol amendments			

	Form FDA 1572 (all versions)			
	CVs for Investigator and Subinvestigators listed on all versions of Form FDA 1572			
	Training records for all key study staff			
IRB files	Approval letter (initial) for initial protocol with original informed consent(s)			
	Amendment approval(s) with approved informed consent(s) (if applicable)			
	Informed consent forms (originals) for enrolled subjects			
	Informed consents for screened subjects			
	Status reports for:			
	• Yearly renewal(s)			
	• Adverse events			
	• Deaths			
	• Study termination			
	• Final summary			
Communications	Sponsor correspondence			
	CRO correspondence			
	IRB correspondence			
	Other study correspondence			
	Monitoring log			
Laboratory	Laboratory certification and normal ranges			
	Drug log to include:			
Drug accountability	• Receipt of drug			
	• Dispensing			
	• Return			
	Equipment log including:			
Equipment accountability	• Receipt of equipment			
	• Dispensing			
	• Return			

3. REVIEW		**YES**	**N/A**	**COMMENTS**
Collect and review for each subject enrolled	CRFs completed for each subject enrolled			
	Data correction forms for CRFs			

	Source documents for each subject enrolled that document the following:			
Medical records and/or study files	• Condition of subject at time of entry into the study (i.e., all inclusion/exclusion criteria are met)			
	• Case history documents including that informed consent process was charted and obtained prior to start of study procedures			
	• Exposure to test article			
	• Concomitant medications			
	• Clinical assessments of the subject during the course of the study			
	• Laboratory reports			
	• Diagnostic tests			
	• Dose modifications			
	• Adverse events/death			
	• Protocol exemptions			
	• Early termination			

4. SITE SPECIFIC		**YES**	**N/A**	**COMMENTS**
Temperature Logs	• Refrigeration			
	• Drug			
Equipment	• Name of equipment goes here			
	• Calibration logs			
	• Inspection reports			
	• Permits			
	• Licensure			