Study Management
SM 304.01

STANDARD OPERATING PROCEDURE
Routine Monitoring Visit

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04 Feb 2021

(Signature and Date)

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04 Feb 2021

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Issue Date:	01 June 2017
Effective Date:	01 September 2020
Expiration Date:	01 September 2022
Document Review Date:	30 June 2020
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1. INTRODUCTION AND PURPOSE

Georgia CORE is responsible for conducting routine monitoring visits periodically for all clinical trials conducted within the Georgia CORE Research Network sites. Routine monitoring visits are conducted to ensure that implementation of the clinical trial are compliant with protocol, federal regulatory requirements, and Georgia CORE policies and procedures. Routine monitoring is essential for the scientific, clinical, and ethical integrity of the clinical trial and safety of trial subjects.

The purposes of routine monitoring visits are to:

- Document and report on the clinical trial progress,
- Document that the protocol and associated CRFs ~~forms~~ are current and accurate,

- Update the Research Network site staff of any changes in the conduct or documentation required for the clinical trial,
- Ensure that Investigator and Georgia CORE obligations are met,
- Ensure continued acceptability of the Investigator and ~~his/her team and facility~~ the Research Network site staff and facilities,
- Review current clinical trial data, reports, and source documents,
- Obtain required documentation for Georgia CORE study files,
- Ensure adequate investigational product inventory and accountability.

2. SCOPE

This SOP applies to all Georgia CORE staff and consultants involved in scheduling, conducting, and reporting on routine monitoring visits for all clinical trials subject to investigation new drug (IND) regulations for drugs and biologics or those eligible for investigational new drug (IND) exemption during all investigational phases of development. For the purpose of this SOP, the term "Investigator" includes both Investigators and Subinvestigators.

3. APPLICABLE REGULATIONS AND GUIDELINES

The Code of Federal Regulations and the International Conference on Harmonization, Good Clinical Practice: Consolidated Guideline apply to this SOP (Appendix A).

4. REFERENCES TO OTHER APPLICABLE SOPS

GA - 204	Site Initiation Visit
SM - 301	Communication
SM - 302	Interactions with the Institutional Review Board
SM - 303	Documentation and Records Retention
SM - 306	Adverse Event Reporting
SM - 307	Investigational Product Management
SM - 308	Specimen Management
DM - 401	Data Management
PP - 501	Safeguarding Protected Health Information

5. ATTACHMENTS

A. Monitoring Site Visit Checklist and Report
B. Screening and Enrollment Log Template
C. Subject Eligibility Criteria Form
D. Investigator Compliance Meeting Summary and Action Items

6. RESPONSIBILITY

The Georgia CORE President and CEO is responsible for designating a trained and qualified Georgia CORE staff member or consultant to serve as monitors for clinical trials conducted within the Georgia CORE Research Network.

This SOP applies to monitors who are responsible for scheduling, preparing for, conducting or participating in, documenting, and reporting on monitoring visits conducted by Georgia CORE.

- President and CEO
- Chief Medical Officer
- Georgia CORE staff and consultants

7. DEFINITIONS

The following definitions apply to this SOP (Appendix B):
Case report form (CRF)
Compliance (in relation to trials)
Contract
Direct access
Documentation
Essential documents
Good Clinical Practice (GCP)
Investigator
Monitoring
Protocol
Protocol amendment
Source documentation
Sponsor
Subinvestigator

8. PROCESS OVERVIEW

A. Frequency and Scheduling of Routine Monitoring Visits
B. Preparing for Routine Monitoring Visits
C. Conduct the Routine Monitoring Visits
D. Following Up after the Routine Monitoring Visit

9. PROCEDURES

A. Frequency and Scheduling of Routine Monitoring Visits*

***Remote Routine Monitoring Visits may be implemented under certain circumstances, i.e., pandemics. Review both Georgia CORE monitoring procedures as well as site procedures for conducting remote visits.**

Georgia CORE staff and consultants	Estimate the number of anticipated routine monitoring visits based on study design, complexity, phase of development, experience of the Research Network site Investigator, previous Research Network site compliance, rate of subject enrollment and any other unique attributes of the study and the Research Network site. Conduct a minimum of one routine monitoring visit at each study site. Some studies may require scheduling the

first routine monitoring visit after the enrollment of the first subject, with additional routine monitoring visits occurring thereafter.

Routine monitoring visits for Georgia NCORP sites who have at least one year of conducting NCTN trials without any previous documented deviations or high staff turnover rates will occur at a minimum of every 6 months.

Contact the Research Network site Investigator or designee regarding scheduling and conducting the monitoring visits. Record discussions on the telephone contact log. (SOP SM 301.01, Attachment A: Telephone Contact Log).

Confirm date and logistics of the routine monitoring visit in writing and provide the Research Network site Investigator with a list of subject charts to be reviewed.

Note: For Georgia NCORP sites, routine monitoring visit case selection will be a minimum of 10% of the annual accrual for each individual Research Network site.

B. Preparing for the Routine Monitoring Visits

Georgia CORE staff and consultants	Review the relevant content of the study and Research Network site files in the Georgia CORE Regulatory Master File prior to the monitoring visit.
	Review the current protocol and informed consent form prior to the monitoring visit.
	Review CRFs for any queries and overdue data to the Research Network site Investigator needing clarification or correction.
	Review previous monitoring reports and NCI corrective and preventive action plan (CAPA) for any outstanding items that were to be addressed prior to or during the next scheduled visit.
	Prepare a list of questions and issues to be checked against source documents or other documents at the site.
	Make copies of the NCI IRB/ICC audit worksheet, Pharmacy Audit worksheet, Patient Case Audit worksheet for the number of cases/protocols that are reviewed.

C. Conducting Routine Monitoring Visits

C1. Overall Study Status

Georgia CORE staff and consultants	Document the monitoring visit by signing a Site Visit Log at the investigative site (SOP SS-204 Site Initiation Visit, Attachment D.)
	Document all findings during the monitoring visit on a Monitoring Site Visit Checklist and Report (Attachment A) or if NCORP the NCI worksheets.
	https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm
	Assess whether the key Research Network site study personnel and facilities continue to be adequate and trained to conduct the study that the Research Network site Investigator adequately involved in the conduct of the study.
	Verify that the Research Network site study files contain all required documents and records and that they are accurate, complete, and current.
	Confirm that the Research Network site Investigator or designee routinely files and forwards essential and required information to other required parties appropriately (e.g. IRB, Sponsors, Georgia CORE).
	Assess subject enrollment rates and examine unexpectedly high or low recruitment.
	Obtain information on subjects who failed to meet inclusion criteria, did not give informed consent, or withdrew from the study for any reason.
	Review Subject Screening and Enrollment Logs (Attachment B) and Subject Eligibility Checklists (Attachment C) to ensure they have been signed and dated by the Research Network site Investigator or qualified designee
	Confirm eligibility of enrolled subjects by review of inclusion and exclusion criteria and completion of study events per protocol.
	Confirm that all subjects have signed the appropriate informed consent form(s) and that informed consent was obtained before any protocol-related procedures were conducted (except those specified in the protocol).

Evaluate status of follow-up plans and visits for subjects (assess all or a sample of subject records) and identify problems.

Confirm that safety and efficacy assessments are conducted per protocol; confirm that serious adverse events have been documented, reported, and followed up on appropriately.

C2. Case Report Form (CRF) and Source Document Review

Georgia CORE staff and consultants

Verify that CRFs are being completed in a timely manner and per protocol requirements by inspecting CRF pages for completeness, accuracy, and consistency with source documentation.

Review all CRFs (or a sample) to ensure they are complete, legible, and consistent with protocol specifications and signed by the Research Network site Investigator

Review and address omissions and queries and ensure corrections are properly made by the Research Network site Investigator or designee prior to the end of the monitoring visit. Unresolved discrepancies will be documented on the Data Clarification Form (DCF), SOP DM-401 Attachment B) and referenced on the Monitoring Site Visit Checklist and Report for follow up (Attachment A).

Note: Monitors may not enter data, correct data, or write on the CRFs.

If a recorded entry on the CRF appears to be incorrect, the monitor will indicate on the monitoring visit report that the entry was verified.

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Track CRF changes, corrections and outstanding queries on the Monitoring Site Visit Checklist and Report (Attachment A).

The following information must be included in the case history for each participant: notice of participation in the study, medical condition being treated, dosage or amount or type of investigational product being administered or used, the approximate duration of therapy, any concomitant therapy, and study events and other relevant information.

	Assess whether all SAEs have been documented and reported as specified in the protocol and other relevant regulatory procedures.

C3. Investigational Products, Supplies, and Storage Monitoring

Georgia CORE staff and consultants	Ensure that investigational product and supply accountability and reconciliation obligations are being followed. Verify all investigational products are within labeled expiration dates. Examine storage refrigerator, freezers, and other storage equipment to confirm they are as required by the protocol and that calibration and temperature logs are maintained in the site study file. Check the Research Network site inventory of investigational product, management forms, or other relevant materials, and arrange to provide additional items as necessary after concluding the visit Evaluate allocation of investigational products and verify that the randomization procedures were carried out per protocol. Determine the inventory of investigational products. Document all findings during the monitoring visit on a Monitoring Site Visit Checklist and Report (Attachment A) or if NCORP the NCI worksheets.

C4. Specimen and Laboratory Monitoring

Georgia CORE staff and consultants	Verify that all specimens for protocol-specific laboratory studies are being collected, processed, stored, packaged, and sent to the appropriate processing sites in a timely manner

C5. Staff and Facilities Monitoring

Georgia CORE staff and consultants	Confirm that the Research Network site Investigator is supervising and participating in the study and assigning and documenting delegation of tasks for the study to Research Network site staff according to his/her training or experience. Assess the ongoing adequacy of Research Network site facilities and staff for conducting the study. Provide or schedule additional study training for new staff.

C6. Communication Records

Georgia CORE staff and consultants	Review any study conduct issues or other incidents of noncompliance with the Research Network site Investigator and other key personnel. Document the issues and follow up plan on the Monitoring Site Visit Checklist and Report. (Attachment A).

C7. Protocol Violation Monitoring

Georgia CORE staff and consultants	Note if the records show any evidence that protocol and violations have occurred and record the nature of the violations on the Monitoring Site Visit Checklist and Report (Attachment A). Review any study conduct issues or other incidents of noncompliance with the Network site Investigator and other key personnel. Document the issues and follow up plan on the Monitoring Site Visit Checklist and Report. (Attachment A).

C8. Conclusion of the Routine Monitoring Visit

Georgia CORE staff and consultants	Meet with the Research Network site Investigator and key staff to discuss any scientific or administrative problems (including study conduct issues or incidents of non-compliance) and possible solutions. Document on the Monitoring Visit Checklist and Report and include a follow up plan (Attachment A). As necessary, remind the Research Network site Investigator that all records and reports pertaining to the study must be retained at the study site as required by the study agreement and applicable regulatory requirements. As necessary, remind the Research Network site Investigator to provide all updated information pertaining to the study including changes in key personnel to the monitor on a timely basis. After concluding the monitoring visit, report any significant unresolved problems or protocol violations immediately to the Research Network site Investigator and the Georgia CORE President, who may confer with the Chief Medical Officer regarding the findings. Provide Attachment D (Investigator Compliance Meeting Summary and Action Items) for use if the meeting is deemed necessary.

D. Following Up after Routine Monitoring Visits

Georgia CORE staff and consultants	Complete Routine Monitoring Visit Report and distribute to the Research Network site Investigator or site, and the Georgia CORE President and CEO. **Note:** For Georgia CORE Research Network sites where the Georgia CORE CMO provides oversight, a copy of the Routine Monitoring Visit will be furnished to the Georgia CORE CMO. Conduct additional monitoring visits as needed. Unscheduled visits may be based on reports or evidence of potential noncompliance with any Sponsor/regulatory requirements (noted during a prior scheduled visit or received from any other source, including employees of the Investigator), significant increases in subject enrollment rates, and/or changes in protocol, personnel, and training activities.

10. HISTORY

Version Number	Section Number	Modification	Approval Date
304.00	All	Original Version	
304.00	All	No change necessary	09 March 2012
304.00	All	No change necessary	01 July 2014
304.00	3, 9A, B, C	Inclusion of NCORP and NCI auditing guidelines	21 March 2017
304.01	All	Edits for clarification, flow of activities, and consistent use of terminology, addition of content in 9D	30 June 2020

ATTACHMENT A:
Monitoring Site Visit Checklist and Report

Protocol Title: _____

Protocol Number: _____ Site Name: _____

Site Sub-PI: _____

Site #:_____ Site Contact:_____ Visit Date:_____

Study Personnel Present During Visit Name(s) and Title(s):

Name_____Title_____
Name_____Title_____
Name_____Title_____
Name_____Title_____

Monitor Name: _____Type of Visit: ☐ Routine/Scheduled
☐ Unscheduled/For Cause:

_____

_____

Subject Status:

Date of First Subject Enrolled _____ Date of Most Recent Subject Enrolled_____

Total # Subjects Enrolled_____ Total # Subjects Planned _____

Subjects Screened _____ Total # Subjects Completed _____

#Subjects Active_____ #Subjects Prematurely Withdrawn _____

#Unanticipated AEs _____ #CRF Collected: To Date _____

#Protocol Deviations_____ #CRF Collected: This Visit_____

FACILITIES/STAFF	YES	NO	N/A	ACTION ITEMS/ISSUES/COMMENTS
Changes in staff?				
If yes, was the study documentation updated?				
If yes, was the staff properly trained for the study?				
Has investigator accepted new studies since last year?				
Is investigator properly supervising other personnel?				
Is investigator devoting enough time for the study?				
Investigator accessible during visit?				
Has facility/work area changed since last visit?				
If yes, was study documentation updated?				
If yes, were the new f facilities/equipment inspected?				
Are treatment facilities adequate?				
SERIOUS ADVERSE EVENTS (SAEs)	**YES**	**NO**	**N/A**	**ACTION ITEMS/ISSUES/COMMENTS**
Any SAEs since last visit?				
If yes, were required forms completed and submitted?				
Outstanding data or forms for this or previous events?				
Were any unreported SAEs discovered?				
IRB informed, if required?				
SUBJECT VERIFICATION AND CRF REVIEW*	**YES**	**NO**	**N/A**	**ACTION ITEMS/ISSUES/COMMENTS**
Protocol requirements being followed:				.
Consent form(s) signed before enrollment?				
Subsequent, applicable consent form(s) signed?				
CRFs reviewed?				

	SUBJECT VERIFICATION AND CRF REVIEW*	YES	NO	N/A	ACTION ITEMS/ISSUES/COMMENTS
	Source documents reviewed?				.
	Was the data collected verifiable?				
	Were there any inconsistencies noted in reviews?				
	Are CRFs completed properly and on a timely basis?				
	Are CRFs legible, accurate and complete?				
	Are other worksheets legible, accurate, and complete?				
	Are the CRF Binders accurate and complete for each patient?				
	CRF problems discussed with staff?				
	CRF corrections made?				
	Were proper CRF correction procedures followed?				
	Subject eligibility confirmed?				
	Subject enrollment log up-to-date?				
	Recruitment on schedule?				
	Did subjects have required lab work, etc?				
	Were any significant laboratory abnormalities discovered?				
	Is follow-up current and properly recorded?				
	Are dropouts/withdrawn subjects documented?				
	Have adverse events been adequately documented?				
	Have there been protocol deviations since last visit?				
	Do site records match up with sponsor records?				
	Completed CRFs collected?				

	INVESTIGATIONAL PRODUCT ACCOUNTABILITY	YES	NO	N/A	ACTION ITEMS/ISSUES/COMMENTS
	Are product storage facilities adequate, secure?				.
	Did the location of product storage change since the last visit?				
	Product forms complete and up to date?				
	Product inventory checked and counted?				
	Is the site product accountability log complete and up to date?				
	Are the patient product accountability log(s) accurate and complete?				
	Study supplies adequate?				
	REVIEW OF SITE REGULATORY BINDER	**YES**	**NO**	**N/A**	**ACTION ITEMS/ISSUES/COMMENTS**
	Protocol – IRB approved				
	Signed protocol signature page				
	Current investigator brochure or packet inserts				
	IRB-approved amendments signed & dated				
	IRB-approved consent(s)				
	IRB letters of approval				
	IRB Annual Report				
	IRB Annual Re-approval letter(s)				
	Safety Updates/Reports submitted to IRB				
	IRB Approved Patient Advertisement/Recruitment Tools				
	IRB correspondence – Annual, SAEs				
	IRB composition				
	Signed and completed FDA 1572				
	Signed and completed revised FDA 1572				
	Safety Updates/Reports submitted to IRB				

	REVIEW OF SITE REGULATORY BINDER	YES	NO	N/A	ACTION ITEMS/ISSUES/COMMENTS
	CVs for PI and sub-investigators				
	CVs for Key site research personnel, e.g. Lab Director				
	Medical Licenses for all Investigator(s) and sub-investigator(s)				
	Financial disclosure forms for investigators				
	Shipping records for investigational products and accountability records				
	Agreements/contracts -executed				
	Agreements/contracts amendments - executed				
	Lab certifications (licenses and accreditation)				
	Lab normal ranges				
	Screening & Enrollment Log				
	Signature Participant Log/Delegation of Responsibility Log				
	Study Monitor Visit Log current				
	Telephone Logs current				
	All pertinent correspondence				
	INVESTIGATOR/MONITORING MEETING	**YES**	**NO**	**N/A**	**ACTION ITEMS/ISSUES/COMMENTS**
	Reviewed all significant findings?				
	Reviewed any unresolved issues and corrected items from previous visits?				
	Discussed results of visits and action items with investigator and staff?				
	Findings provided to the site in writing?				
	Appointment made for next visit?				
	Reviewed all significant findings?				
	Reviewed any unresolved issues and corrected items from previous visits?				
	Discussed results of visits and action items with investigator and staff?				

	OVERALL REVIEW OF STUDY STATUS	YES	NO	N/A	ACTION ITEMS/ISSUES/COMMENTS
	Is maintenance of records complete?				
	Is site in compliance with protocol and IRB?				
	Are subjects accruing within timelines?				
	Is additional clinical/technical training required?				

*Subject Verification and CRF Review
If all subjects cannot be reviewed, select a statistically valid number of subjects for complete review. List selected CRFs by subject's identification code below. List inconsistencies in table and discuss in the appropriate comment section.

_____ _____ _____ _____ _____ _____ _____

_____ _____ _____ _____ _____ _____ _____

SUMMARY OF FINDINGS:

Findings	Action Item	Resolved	
		Yes	No

SUMMARY:

Recommendations of Monitor

☐ No action needed – study conduct is compliant with regulations, protocol and IRB requirements

☐ No action required, but visit site again in _____ weeks to ensure corrections have been made

☐ Action required: Investigator is noncompliant, schedule review meeting

☐ Action required: Terminate study at site

Monitor Signature and Date:_____

Recommendations of Principal Investigator and/or President and CEO

☐ I agree with the recommendations of the monitor

☐ I do not agree with the recommendations of the monitor

Reason:

_____

_____

_____

_____

Principal Investigator and/or President and CEO Signature and Date:

_____

cc: PI (with original CRFs), Site, Georgia CORE regulatory files

ATTACHMENT B:
Screening and Enrollment Log Template

Protocol:				**Investigator:** **Site Name:** **Site Number:**				
Screening Number	**Patient Initials**	**Patient Date of Birth**	**Date Screened**	**Date of Informed Consent**	**Date of HIPAA**	**Patient Number (if enrolled)**	**Date of Enrollment**	**Screening Failure Yes/No**

ATTACHMENT C:
Subject Eligibility Criteria Form

Protocol Name/Number: _____		
Investigator Name: _____	Phone: _____	Site: _____
Patient ID: _____	Patient Initials: _____	Gender: _____
Eligible: Yes ☐ No ☐ (See Instructions Below) If not eligible, provide reason: _____		
Screened by: _____ Signature: _____ Date: _____		

INCLUSION CRITERIA (To be eligible, all must be answered Yes)	**Yes**	**No**
1.	☐	☐
2.	☐	☐
3.	☐	☐
Etc.	☐	☐

EXCLUSION CRITERIA ***(To be eligible, all must be answered No)***	**Yes**	**No**
1.	☐	☐
2.	☐	☐
3.	☐	☐
Etc.	☐	☐

Review by Investigator:_____

Signature: _____ Date: _____

INSTRUCTIONS

Include the dates of any test results addressed in the criteria.

If the Investigator or designee determines the participant meets the protocol eligibility criteria, he/she must mark 'Yes" in the section marked "Eligible" at the top of the form, and complete the "Screened by" section.

If the Investigator or designee determines the participant does not meet the protocol eligibility criteria, he/she must mark 'No" in the section marked "Eligible" at the top of the form, document the reason for ineligibility, and complete the "Screened by" section.

If a designee completed the Participant Eligibility Checklist and made the eligibility determination, the Checklist and final determination must be reviewed and approved by the Investigator.

ATTACHMENT D:
Investigator Compliance Meeting Summary and Action Items

Investigator: _____ Protocol #:_____

Date(s) of non-compliance:_____ Date of meeting: _____

Reviewers:

Name	Title
_____	_____
_____	_____
_____	_____
_____	_____

Information Reviewed

_____ Monitoring Visit Checklist and Report(s) Dated _____
_____ Case Report Forms
_____ Other _____

Specific Noncompliance **Comment/Discussion**

_____ Failure to report serious or life-threatening AEs

_____ Serious protocol violations

_____ Repeated or deliberate failure to obtain adequate informed consent

_____ Falsification of study safety data

_____ Failure to obtain IRB approval before
- _____ Initiating study procedures
- _____ Initiating significant protocol changes

_____ Failure to adequately supervise the trial such that subjects are or may be exposed to unreasonable and significant risk of illness or injury

_____ Repeated or deliberate failure to:
- _____ Limit use of the study article to subjects who are under the investigator's supervision
- _____ Comply with conditions placed on the study by the IRB, Sponsor or FDA
- _____ Follow the investigator statement or protocol
- _____ Maintain accurate study records
- _____ Falsification or concealment of study records
- _____ Repeated or deliberate failure to adequately supervise the trial to a degree that subjects may be exposed to an unreasonable significant risk

Findings:

_____ Is noncompliant _____No _____Yes
Investigator Name

The compliance is _____Not Serious _____Serious

Action(s) (Check all that apply):

_____ Secure compliance by: _____ Retraining _____ Increased Monitoring

_____ Conduct audit within _____ days/weeks

_____ Suspend study at site as of _____

_____ Discontinue shipment of product as of _____

_____ Terminate study at site as of _____ and notify FDA by _____

Completed by:

_____ _____
Signature Date

Reviewed by Georgia CORE President and CEO

_____ I agree with the recommendations of this determination

_____ I do not agree with the recommendations of this determination.

Reason:

_____

_____

_____

_____

_____ _____
Signature Date