SOP Number GCP 09
SOP NAME Site Performance Monitoring, Audits and Inspections
Effective Date: 9-Sep-2016 (rev 10-Aug-23)

1. POLICY

The purpose of this Standard Operating Procedure (SOP) is to review policies and procedures for access to electronic and other forms of medical records for research purposes, as well as outline the steps for site performance monitoring during study initiation, data collection and closeout.

2. DEFINITIONS AND ABBREVIATIONS

Abbreviations:

CIRB	Central Institutional Review Board
CRF	Case Report Form
EMR	Electronic Medical Record
FDA	Food and Drug Administration
HIPPA	Health Insurance Portability and Accountability Act
ICD	Informed Consent Document
NCC	National Coordinating Center at the University of Cincinnati
NDMC	National Data Management Center at the Medical University of South Carolina
NINDS	National Institute of Neurological Disorders and Stroke
PHI	Protected Health Information
PI	Site Principal Investigator
PPI	Overall Protocol Principal Investigator
PS	Performance Site
RCC	Regional Coordinating Center
SOP	Standard Operating Procedure
StrokeNet	NIH StrokeNet Network
UPIRSO	Unanticipated Problems Involving Risks to Subjects or Others

Definitions:

Audit – Any inquiry by entities overseeing research conduct such as NINDS, NCC, NDMC, FDA, or CIRB to ensure compliance with study specific, institutional and national laws, regulations, policies and procedures. This includes routine inspections of data quality, study procedures, maintenance of records and human subjects protection.

Source Data – All information in original records and certified copies of original records of clinical findings, observations or other activities in a clinical investigation used for reconstructing and evaluating the investigation.

Source Data Verification – Review of source data by the auditor or NDMC appointed monitor to ensure the quality, accuracy and integrity of the clinical investigation data and adequate protection of the rights, welfare and safety of human subjects.

Study Close-out – The process by which StrokeNet, the trial PPI and/or trial sponsors and other relevant agencies determine that applicable administrative actions and other work specified in the protocol has been completed.

Study Initiation – The process by which StrokeNet, the trial PPI and/or trial sponsors and other relevant agencies determine that a site is ready to begin implementing a protocol.

3. SCOPE

This SOP applies to the management of source documents and electronic medical records (EMR) collected for StrokeNet research purposes by network investigators, site trial investigators and staff, subcontractors or other entities associated with StrokeNet. Additionally, this SOP outlines the procedures for site performance and Human Subjects Protection monitoring and applies to all StrokeNet affiliated staff members that manage, oversee, and conduct research within the network.

4. PROCEDURES

A. Access to Paper Records and EMR
   1. Information from EMR will be used in research studies provided that access is specifically designated and limited to those directly participating in research. A Performance Site (PS) EMR system must demonstrate 21 CFR Part 11 compliance or be able to provide a certified copy of the accurate and complete medical record for the purpose of trial related inspections. Records containing Protected Health Information (PHI) may be accessed prior to approval of a protocol with local Institutional Review Board approval for research

preparatory purposes including identifying potential study populations, provided this PHI is not removed from the institution or disclosed to another entity.

2. Research personnel responsible for abstracting data from original records at a PS, with guidance from Regional Coordinating Center (RCC) staff, will serve as a liaison between researchers, biostatisticians and other personnel including outside investigators, site monitors or auditors to monitor or verify source data information for StrokeNet affiliated research. Direct EMR data extraction for research should be approved by the Central Institutional Review Board (CIRB) to ensure all human subject protections, Health Insurance Portability and Accountability Act (HIPAA) regulations and other federal, state and local laws are being followed. Prior to beginning data collection, researchers should provide documentation of the personnel who will be allowed to access the extracted data and the required level of access (for example, access to PHI).
3. EMR data must be accessed by pre-specified personnel for auditing and data verification purposes. Each PS can define the process by which this is achieved in their institution. Research studies may be periodically monitored by sponsoring agencies and other appropriate personnel for the purposes of ensuring that human subject protections are being followed, trial data are accurate and complete and that the study is being conducted according to the protocol and other established approval guidelines. Prior to a monitoring visit, the PS will be notified of the purpose, proposed date and nature of the data to be monitored. The PS PI/delegate will assure that all research data, source data and regulatory documents necessary to conduct the monitoring visit are available for review. If using a research pharmacy or a clinical pharmacy providing service for research studies, the pharmacist will facilitate inspection of investigational product storage, and the applicable accountability logs. StrokeNet PS personnel will be expected to comply with all local/institutional requirements to obtain appropriate approvals to release the necessary data.

B. Policies for StrokeNet Site Monitoring

All trial specific PS monitoring is conducted by trained, qualified personnel overseen by the National Data Management Center (NDMC) or other trial specific or StrokeNet affiliated staff who are familiar with the protocol. The type of monitoring is either determined by the phase of the trial, or by pre-specified parameters to ensure data quality, proper documentation and/or participant safety. The PS PI and relevant research personnel should be accessible at all monitoring visits.

1. **Site Initiation and Training Visits:** The purpose of a site initiation visit is to orient and train staff on the study protocol and other study procedures, to confirm that the site is ready to begin recruitment and to identify additional resources or actions are needed prior to starting the study. In addition, the designated trial or network staff performing the visits will check to make sure all facilities have met the safety requirements for conducting a

trial. Ideally all CIRB, contractual and regulatory requirements have been met or addressed prior to an initiation visit**.** These visits may occur remotely or in-person.

a. Prior to a trial site initiation visit the PS should:
    1. Assure the study protocol has been approved by the CIRB and complete all necessary PS ancillary reviews.
    2. Review all identified trial specific study staff roles.
    3. Complete any other network, trial PPI or RCC specified site initiation procedures.

2. Routine Data Monitoring Visits: NDMC monitoring visits are conducted periodically to protect data quality, to ensure that accuracy of collected data and to monitor that all data collection procedures are being followed according to the protocol. These visits may occur remotely or in-person.

a. For a routine data monitoring visit the PS should be aware:
    1. Documentation should comply with Good Documentation Practice standards and Good Clinical Practice principles established by the network.
    2. Paper or electronic source data must be available to be checked against electronic case report forms (CRFs) entered into the WebDCU™ database for accuracy.
    3. Adverse events should be documented and reconciled per the requirements of the trial.
    4. Medication dosage information may be verified for trial participants.
    5. Missing information, participant withdrawals and non-compliance must be accurately documented and reported.
    6. Deviations from protocol must be properly recorded, filed and reported to the CIRB, and to the local IRB if local requirements dictate, according to StrokeNet policies and trial specific guidelines.
    7. WebDCU™ data queries for missing information or errors found in electronic CRFs or other records must be addressed.
    8. The PS PI and research personnel must be available to meet with site monitors to review findings and discuss action items.

3. Performance Monitoring Visits: These visits will be conducted by PPI, NCC, or NDMC staff to observe adherence to protocol, address issues such as recruitment or in response to a concern about participant safety. These visits may occur remotely or in-person.

a. During such a visit PS should be prepared to:
    1. Review recruitment and enrollment numbers, as well as materials and procedures used for recruitment and screening.
    2. Review requested trial documents such as participant records, Informed Consent Documents (ICDs), protocol approvals and amendments.

4. **Auditing Visits:** Any entity overseeing research conduct such as NINDS, NCC, NDMC, FDA, or CIRB may conduct an auditing visit to ensure compliance with study specific, institutional and national laws, regulations, policies and procedures. This includes routine inspections of data quality, study procedures, maintenance of records and human subjects protection. These visits may occur remotely or in-person.
    a. During such an audit the PS should be prepared to:
        1. Provide documentation of locally maintained regulatory and event reporting records.
        2. Provide paper or electronic source data to be checked against electronic CRFs entered into the WebDCU™ database for accuracy.
        3. Provide access to EMR as needed.
        4. Provide access to other requested trial documents such as training, screening, pharmacy or laboratory records.
        5. Notify the NCC and NDMC upon request of an auditing visit by another entity, and provide the NCC and NDMC with a copy of the final report upon conclusion of the auditing visit.
5. **Study Close-out:** A study close-out visit may occur at the end of a trial, to ensure that all administrative actions and study procedures have been completed, data has been entered and all other requirements of the study protocol have been met including disposition of investigational product. These visits may occur remotely or in-person.
    a. At a close-out visit the PS should be prepared to:
        1. Resolve any final or outstanding data queries or adverse events.
        2. Perform final accountability and shipping or destruction of remaining investigational product, if required.
        3. Assure appropriate labeling and storage of all study data.
        4. Notify CIRB of site closure and assure all documentation with CIRB (including regarding Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO) or other unanticipated events) are retained at the PS with other study records.

C. Non-compliance or negligence

If any serious deviations from study procedures or safety protocols are found on the part of the institution, study staff or investigator; the StrokeNet leadership, the trial sponsor or the CIRB acting collaboratively may terminate that institution's participation in the trial.

5. APPLICABLE REGULATIONS AND GUIDELINES

ICH E6 (R1)-5.19 Audit

ICH E6 (R1)-6.10 Direct Access to Source Data/Documents

21 CFR Part 11 Electronic Records: Electronic Signatures

21-CFR 312.62 Investigator Record Keeping and Record Retention

National Institutes of Neurological Disorders and Stroke Policies and Guidelines
http://www.ninds.nih.gov/research/clinical_research/policies/mop.htm

Guidance for Industry, Electronic Source Data in Clinical Investigations Sept 2013

6. REFERENCES TO OTHER APPLICABLE SOPS

ADM #12 CIRB Reporting

GCP #4 Safety Reporting

GCP #5 Maintaining Confidential Information

GCP #12 Regulatory and Clinical Data Maintenance and Data Storage

7. ATTACHMENTS AND REFERENCES

Good Documentation Practice: http://ec.europa.eu/health/files/eudralex/vol-4/chapter4_01-2011_en.pdf

HIPAA Regulations: http://www.hhs.gov/ocr/privacy/hipaa/understanding/index.html

National Institutes of Health, Clinical Research and the HIPAA Privacy Rule:
http://privacyruleandresearch.nih.gov/clin_research.asp

National Institutes of Neurological Disorders and Stroke Glossary of Clinical Research Terms
http://www.ninds.nih.gov/research/clinical_research/basics/glossary.htm

8. DOCUMENT HISTORY

Version	Description of Modification	Completion Date	Issue Date	Effective Date
0.1	Draft of GCP #9	4/28/2014		**Upon date of last signature**
0.2		6/23/2016 JF		
0.3		6/24/2016 JAS		
0.4		8/29/2016 CD		
1.0	Final	9/9/2016	9/9/2016	9/9/2016

2.0	Administrative review	6-Jul-23	10-Jul-23	10-Jul-23
2.1	NDMC review	10-Aug-23	10-Aug-23	10-Aug-23