SOP Number GCP 09
SOP NAME Site Performance Monitoring, Audits and Inspections
Effective Date: 9-Sep-2016

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

CRF	Case Report Form
CPS	Clinical Performance Site
EMR	Electronic Medical Record
FDA	Food and Drug Administration
HIPPA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
cIRB	Central Institutional Review Board
NCC	National Coordinating Center
NDMC	National Data Management Center
PI	Site Principal Investigator
PPI	Overall Protocol Principal Investigator
RCC	Regional Coordinating Center
SOP	Standard Operating Procedure
StrokeNet	NIH StrokeNet

Definitions:

Audit – any inquiry by NINDS, NCC, NDMC, FDA, or cIRB conducted 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 participant safety.

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

Source Data Verification – review of data source by the 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.

Research Data Coordinator – Individual at the CPS who responsible for data extraction from original records or electronic medical record systems for research purposes.

Protected Health Information – Individually identifiable health information

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 EMR for research purposes under the StrokeNet, including that collected by all 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 includes all StrokeNet affiliated staff members that manage, oversee, and conduct research within the network regulated by the network, FDA and/or applicable review committees.

4. Procedures

A. Access to Paper and Electronic Medical Records (EMR)

1. Information from electronic medical records will be used in research studies provided that access is specifically designated and limited to those directly participating in research. A clinical trial site institution EMR must have demonstrated 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 IRB 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. A CPS research data coordinator with guidance from RCC staff will serve as a liaison between researchers, biostatisticians and other personnel including outside investigators or auditors to extract, monitor or verify the necessary EMR and other paper source information for StrokeNet affiliated research. Direct EMR data extraction for research should be approved by the cIRB to ensure all human subject protections, HIPAA regulations and other federal, state and local laws are being followed. Prior to beginning data collection, researchers should provide documentation of who will be allowed to access data and level of access (for example, access to PHI).
3. EMR data must be accessed by non-site personnel for data verification purposes.

Each CPS 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 site performance or other monitoring visit, the CPS will be notified of the purpose, proposed date and nature of the data to be monitored. The CPS site PI/delegate will assure that all data, source 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 IP storage, and the applicable accountability logs. StrokeNet CPS will be expected to comply with all local/institutional requirements to obtain appropriate approvals to release data.

B. Policies for Site monitoring/Audits/Inspections

All trial specific CPS monitoring is conducted by trained, qualified personnel overseen by the NDMC or other trial specific or network affiliated staff who are familiar with the protocol of the specific study. The type of monitoring is either determined by the phase of the trial, or by a specific need to ensure data quality, proper documentation and/or participant safety. The CPS PI, research data coordinator, and study program coordinators should be accessible at all monitoring visits.

1. **Site Initiation and Training Visits:** The purpose of a monitoring visit for site initiation is to orient and train staff on the study protocol and other manuals of procedure; to confirm that the site is ready to begin recruitment; and to identify what additional resources are needed, or other requirements need to be made 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**.**
    a. Prior to a trial site initiation visit the CPS should:
        1. Assure the study protocol has been approved by the cIRB and has completed all necessary CPS ancillary reviews.
        2. The RCC, NCC project manager, and CPS staff must have reviewed all identified trial specific study staff roles.

3. Any other network, trial PPI or RCC specified site initiation procedures should be specified and followed.

2. **Routine Data Monitoring Visits:** NDMC Monitor 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. Additionally during a data verification visit, original signature informed consent forms (ICFs) may be examined to verify all subjects have provided written consent for participation in the trial.
   a. For a routine data monitoring visit the CPS should be aware:
      1. Documentation should comply with Good Documentation Practice standards and GCP principles established by the Network,
      2. Data from EMR or other electronic or paper sources documents must be available to be checked against the 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,
      7. WebDCU™ data queries for missing information or errors found in eCRFs or other records must be addressed,
      8. The CPS PI and research data coordinator 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.
   a. During such a visit CPS should be prepared to:
      1. Review recruitment and enrollment numbers, as well as materials and procedures used for recruitment and screening,
      2. Review trial documents if requested including participant records, ICFs, approved protocols and amendments signed and dated, any other required reports.
4. **Human Subject Protection Monitoring Visits:** Any research involving human subjects may be audited. Quality assurance and improvement activities are applied to all researchers, departments, and units engaged in cIRB approved human subjects' research, including those whose research is conducted at any locations affiliated with a StrokeNet CPS. Upon execution of a Reliance Agreement the cIRB will work with the relying institution to assure compliance with cIRB determinations and StrokeNet procedures for reporting to the cIRB.

a. During such an audit the CPS should be prepared to:
    1. Provide documentation of locally maintained records of required cIRB event reporting,
    2. Provide access to EMR as needed to assure compliance with cIRB determinations.

5. **Study close-out:** A study close-out visit occurs 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.
    a. At a close-out visit the CPS should be prepared to:
        1. Resolve any final or outstanding data queries or adverse events,
        2. Perform final IP accountability and shipping of remaining IP, 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 to Others (UPIRSO) or other unanticipated events) are retained at the CPS 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

GCP #4 Safety Reporting

GCP #5 Maintaining Confidential Information

GCP #7 Maintaining Data Quality

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	Justification for Modification	Completion Date	Issue Date	Effective Date
0.1	Draft of GCP #9	Initial draft of GCP #9 for NCC	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