NIH StrokeNet Network
Standard Operating Procedure

SOP Number: ADM 17
SOP NAME: NIH StrokeNet Organization and Governance
Effective Date: 6-Nov-2015

1. POLICY

The purpose of StrokeNet is to develop and conduct high-quality, multi-site phase 1, 2 and phase 3 clinical trials focused on key interventions in stroke prevention, treatment, and recovery. This document is to provide definitions and explanations of the responsibilities for the components of the NIH Stroke Trials Network (StrokeNet).

2. ABBREVIATIONS AND DEFINITIONS

cIRB	Central Institutional Review Board: Assumes the responsibility of approving, monitoring and reviewing biomedical and behavioural research involving humans.
PS	Performance Site: An institution that is not legally affiliated with an awarded RCC but which has agreed to serve and be wholly supervised by the RCC as a network trial recruitment site.
CTSA	Clinical and Translational Science Awards: A program that aims to strengthen and support translational research by accelerating the process of translating laboratory discoveries into treatments, training new clinical and translational researchers, and engaging communities in clinical research efforts.
DSMB	Data and Safety Monitoring Board
EC	Executive Committee: A governance committee of StrokeNet
EM/EMS	Emergency Medicine/Emergency Medical Services
fCOI	Financial Conflict of Interest
fCOI-C	Financial Conflict of Interest Certification
FDA	Food and Drug Administration
GCP	Good Clinical Practice: Is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects.
IDE	Investigational Device Exception: Allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data
IND	Investigational New Drug: New drug or biologic that is used in a clinical investigation
LONI	Laboratory of Neuroimaging: Imaging repository for all StrokeNet studies
MTA	Master Trial Agreements
NDMC	National Data Management Center at the Medical University of South Carolina
NCC	National Coordinating Center at the University of Cincinnati
PM&R/PT	Physical Medicine and Rehabilitation /Physical Therapy
PPI	Protocol Principal Investigator
RA	Reliance Agreement
RCC	Regional Coordinating Center: An institution designed and directly funded by the NINDS/NIH to provide leadership for the NSN on a regional level.
SS	Satellite Site: an institution named by an RCC as a part of its regional network that is not legally affiliated with the RCC but maybe delegated (via RCC standard operating procedures (SOPs) certain leadership responsibilities.
StrokeNet	NIH StrokeNet Network

WG	Working Group: A stroke domain review committee of StrokeNet
WebDCU™	Comprehensive clinical trials management system operated by NDMC

3. SCOPE

The information provided in this document applies to all internal and external StrokeNet interfaces.

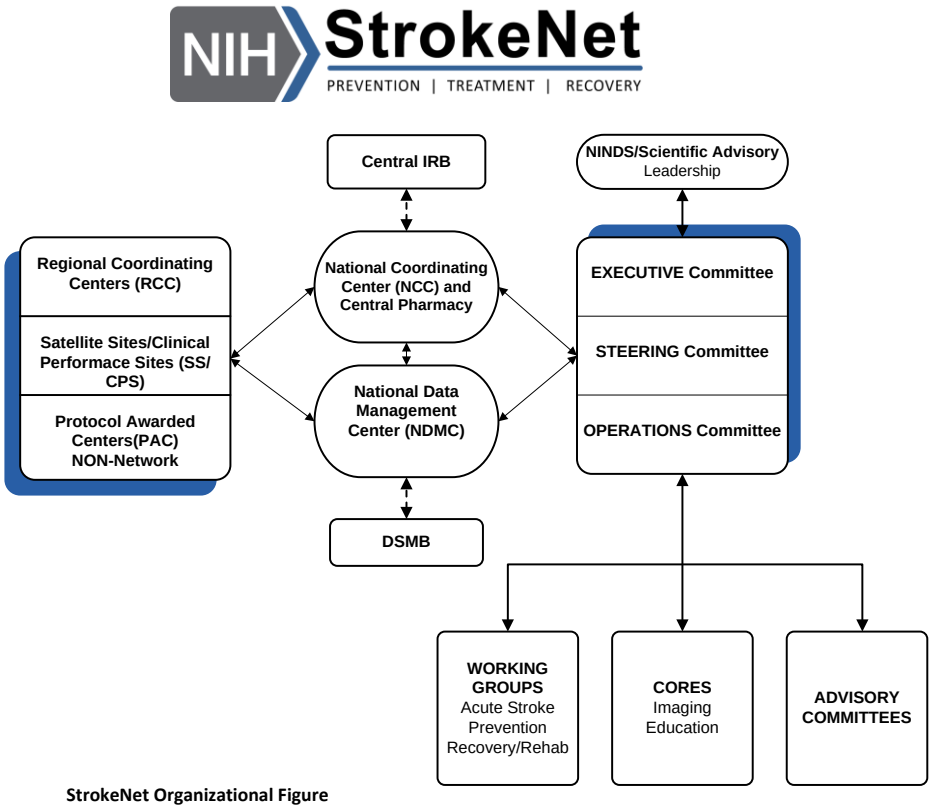
4. PROCEDURES

A. Overall Network Structure and Components

The StrokeNet is comprised of the NCC, the NDMC, cIRB, and the Central Pharmacy and at least 25 RCCs each with multiple affiliated SS and/or PS. The StrokeNet operating structure noted is supported by the National Institutes of Health under infrastructure awards to the NCC, the NDMC and to each RCC. The cIRB and Central Pharmacy are funded under the NCC award.

StrokeNet is governed but two primary committees - the Executive and Steering Committees. The Operations Committee provides conduct and/or oversight for Network activities.

There are three permanent WGs representing three primary stroke research domains: Primary and Secondary Stroke Prevention, Acute Stroke Treatment, and Recovery and Rehabilitation. Two standing core groups are the Education and Imaging Cores.



StrokeNet Organizational Figure

In addition to serving in advisory roles to the overall network and to the WGs are multiple Internal Advisory committees: Clinical and Translational Science Awards (CTSA), Neuro-Interventional, Cerebrovascular, Emergency Medicine/Emergency Medical Services (EM/EMS), Physical Medicine and Rehabilitation/Physical Therapy (PM&R/PT), Neuro-critical Care, Telemedicine, Minority Recruitment, Pediatric Stroke, Biomarkers and Preclinical Science.

B. The National Coordinating Center (NCC)

The NCC provides leadership for the StrokeNet infrastructure to facilitate rapid development and implementation of NINDS-funded stroke trials. Responsibilities of the NCC include but are not limited to:

1. Network support: Provide fiscal oversight and budget development, establish and monitor Human Subject Protection and equality of minority and gender representation thru the establishment of a cIRB, management of investigational products and distribution services through Central Pharmacy services, issue and maintain standard MTA and RAs with RCCs and appropriate SS and PSs, coordinate communication within the network both electronically and in-person.
2. Project Management Support: Assist PPI or other IND sponsor as needed with protocol development, finalization and amendments to facilitate FDA and DSMB regulatory approval, disseminate DSMB, FDA and cIRB approved protocols and amendments to StrokeNet sites, develop protocol specific policies, guidelines and Manual of Procedures (with PPI). Participate in development of an effective safety monitoring plan. Provide and manage cIRB review for StrokeNet protocols and provide for drug and or device distribution as required by the protocol.
3. Site Management Support: Distribute to the sites per subject payments in collaboration with the trial sponsor and provide cIRB review of site provided regulatory documents for completion and accuracy, perform site initiation, regulatory audit and closeout visits, review and distribute trial site performance reports, provide training in Good Clinical Practice (GCP) and outcome assessments in collaboration with cIRB and trial sponsor and disseminate IND safety reports.

C. The National Data Management Center (NDMC)

The NDMC has primary authority and responsibility to develop, implement and maintain the data management and statistical activities necessary for rapid development and implementation of NINDS funded trials. Responsibilities of the NDMC include but are not limited to:

1. Database Development- Using the WebDCU™ system, develop, implement and maintain a central database that streamlines and maximizes efficiency in data collection, processing, and monitoring of clinical, biomarker and neuroimaging data, and in trial management that will provide full support for all study operation activities in the Network, while ensuring compliance with the NINDS Stroke Common Data Elements and FDA regulations.
2. Data Management- Train Network personnel on using the WebDCU™ system; coordinate data management and trial operations, and provide data quality control and assurance through multiple approaches, including risk-based central and on-site monitoring. Prepare and disseminate study data for public use and facilitate data sharing across studies.
3. Statistical Collaboration- Develop and/or contribute to the innovative and efficient study design development. Statistically monitor the study progress. Generate reports for the DSMB and statistical tables for the reports to the FDA, NINDS, and ClinicalTrials.gov. Conduct interim analyses and lead or participate in the final analysis. Collaborate in the dissemination of study results via presentations and publications.

D. The Regional Coordinating Center (RCC)

The RCCs have primary authority and responsibility to develop, implement and maintain a Regional Network of trial execution sites necessary to facilitate rapid development and implementation of NINDS funded trials. Responsibilities of the RCC include but are not limited to:

1. Recruiting SS and PS and for providing scientific leadership and regular communication to SS and PS regarding protocols and study progress and for providing administrative and budget support for protocol initiation.
2. Providing leadership for StrokeNet activities including implementation of cIRB, establishing MTAs and RAs and cIRB functions at SS and PS, Development of Regional Standard Operating Procedures (SOP) describing interactions and management between RCC and SS and PS, monitoring performance quality and quality control and participation in StrokeNet activities, publications and interactions network and non-network investigator activities.

E. StrokeNet Governance

1. The Executive Committee oversees strategic StrokeNet leadership and overall network management (monitor site performance, extra and intra network collaborations, training, new study opportunities).
    a. Membership**-** Standing members are the NINDS Project Scientist, NCC PI and the 2 Co-PIs, NCC Administrative Director, NCC Sr. Project Manager, NDMC PI, NDMC Co-PI, NDMC Operations Director, Chairs of the Prevention, the Acute Stroke Treatment, and the Recovery and Rehabilitation Working Groups. Rotating members are three RCC PIs chosen in collaboration with NINDS for a three-year term. A current list of members is available from the NCC.
    b. Meetings and Teleconference Frequency**-** Bi-monthly teleconference and bi-annual face to face meetings. Agendas will be provided and minutes of the calls maintained by NCC. Attendance and participation will be recorded by NCC.
    c. Sub-Committees
        a. Publication Committee and Data Sharing Committee
            a. Membership- NCC PI, NDMC PI, NINDS Project Scientist, Chairs of the WGs, Chair of the Imaging Core, the PPI of each ongoing Trial within StrokeNet until the trial is completed. For publications related to education activities the chair and Co-Chair of the Educational Core will be ad hoc members.
            b. Responsibilities- Developing and disseminating knowledge derived from StrokeNet and if appropriate, other network managed studies, updating or amending the Publication and Data Sharing Network SOPS/guidelines and in collaboration with trial PPIs–developing specific publication instructions. The committee does not have authority over individual study Publications Committees except where multiple StrokeNet trials are to be used.
            c. Meetings and Teleconference Frequency**-** As needed in response to publication volume.

b. Conflict of Interest Committee (ad hoc)- Sub-committee of the Executive Committee that monitors issues of conflict of Interest arising within the StrokeNet.
    a. Membership- NCC PI, the UC COI official and a member of the Executive Committee delegated by the NCC PI.
    b. Responsibilities- Review all fCOI forms indicating reportable fCOI and any cIRB management plans developed by the cIRB on behalf of a StrokeNet protocol.
    c. Meetings and Teleconference Frequency- Annually or as needed.

2. The Steering Committee- the main governing body of the StrokeNet's scientific operation and conduct. All major StrokeNet decisions will be determined by majority vote of this committee. Each RCC, the NCC, the NDMC will provide one vote each. All decisions must be concurred by NINDS leadership.
    a. Membership- NINDS Project Scientist, a NCC PI, a NDMC PI, and RCC PIs. A current listing of members is available from the NCC.
    b. Meetings and Teleconference Frequency- Teleconferences will be scheduled monthly. Agendas will be provided and minutes of the calls maintained. Attendance is mandatory but appropriate delegates may be appointed for unavoidable absences. Attendance and participation will be recorded by NCC.
    c. Sub-Committees- none
3. Operations Committee- a non-governing committee that oversees all StrokeNet activities, operational issues and monitors network performance.
    a. Membership- NINDS Program Director, NCC PI, Administrative Director and Sr. Project Manager, NDMC Operations Director and Project Manager, key NCC personnel representing cIRB, central pharmacy and financial administration and contract services, protocol specific PIs and trial specified designees for StrokeNet trials. A current listing of members is available from the NCC.
    b. Meetings and Teleconference Frequency- Teleconferences will be scheduled weekly. Agendas will be provided and minutes of the calls maintained by NCC.
4. Standing StrokeNet WGs (Primary and Secondary Prevention, Acute Stroke Treatment and Recovery and Rehabilitation). The primary function of the WGs is to critique, refine and to assist in determining feasibility for clinical concepts submitted to StrokeNet for review by NINDS or trial proposals developed by StrokeNet investigators.
    a. Membership- Each WG has 14 members. A Chair and a Co-Chair, an NDMC appointed representative, an Imaging Core appointed representative, a volunteer Study Coordinator representative, and nine RCC volunteer PIs appointed by the NCC PI. Each Committee Chairman is provided with a contact list of members by the NCC. Terms for the 10 volunteer (RCC and SC members) will be limited to three years. Potential advisors and ad hoc members will be appointed by the NCC PI.
    b. Responsibilities- the WG clinical concept assessment responsibilities noted above will be managed by the WG chair or an appropriate delegate. Each task of the WG in the assessment process will be defined by the chairman and a timeline for completion provided. The Chairs are also responsible for providing the NCC with a

yearly summary of activities, accomplishments and goals for the coming year within stipulated time frames.

c. Meetings and Teleconference Frequency- the WG Chair is responsible for establishing teleconferences on an as needed basis. Each WG chairman is provided access to a teleconferencing line with their own passcode. Chairs or their designees are required to maintain attendance and written summaries or minutes for group calls. WG face to face meetings may occur in conjunction with StrokeNet meetings on an as needed basis.

d. Subcommittees**-** The working groups are expected to have trial-specific subcommittes who will be responsible for doing much of the data gathering for a specific trial that would be presented to the full working group. However, use of subcommittees to distribute work will be at the discretion of the Chair of the Working Group.

e. Term Limits and Rotation of Working Group Members- the 10 volunteer members will serve no more than six consecutive years. Terms will last for no more than three years, with one-year renewal up to six years maximum. One third of each working group will rotate off each year. The three members to be chosen to rotate off will be chosen randomly. Nominations for new group members will be requested from each RCC for membership in all three Working Groups, and nominations should include CVs. Selection to the working group will be made randomly, minus the RCC members who have rotated off and those who already serve on committee. After preliminary assignments, every effort will be made by Working Group Chairs and the PI of the NCC to ensure representation of all RCCs on one of the three Working Groups.

F. Internal Core Mission Resources:

1. Training and Educational Core- Implements StrokeNet-wide educational activities and mentoring programs with StrokeNet fellows, trainees, faculty and coordinators in collaboration with other networks.
    a. Membership- NCC PI appointed Chair and Co-Chair, faculty, Coordinators, Fellows-Trainees, Educational Coordinator and NINDS Project Scientist.
    b. Responsibilities- Guidance for the network regarding expectations of Fellows-Trainees. Implement educational resources/didactics, develop core curriculum of webinars, and develop ideas for innovation in stroke education.
    c. Meetings and Teleconference Frequency**-** Teleconference calls will be scheduled and additional meetings as needed. Face to face meetings may occur at other StrokeNet meetings. Chairman or delegates will maintain meeting minutes and attendance.
2. Imaging Core- Oversees the imaging component of trials conducted by the StrokeNet. The Imaging Core services will include imaging storage, image analysis and central reading process for StrokeNet protocols coordinated thru the NDMC. It also provides expertise, support and feedback during the protocol review phase.

a. Membership- Chair and Co-Chair: appointed by NCC and NDMC PIs, five imaging experts from the NCC/NDMC and 4 members selected by the Chair of the Imaging Core from interested investigators at the RCCs. Membership may change in collaboration with the chair?
b. Responsibilities-The Laboratory of Neuro Imaging at University of Southern California is responsible for receiving, uploading, compiling, assessing quality and storing all mandated images for the trials run through the StrokeNet. Establish standardized procedures for collection, tracking, evaluation, and analysis of neuroimaging and submit the interpreted data to the WebDCU™. Provide input into neuroimaging components of StrokeNet trials. Each working has an assigned imaging core member.
c. Meetings and Teleconference Frequency- Teleconference calls will be scheduled and additional meetings as needed. Face to face meetings may occur at other StrokeNet meetings. Chairman or delegates will maintain meeting minutes and attendance.

G. **Internal Advisory Committees-** Provide consultative expertise in areas needed to cover the spectrum of potential Clinical Stroke Trials.
1. Standing Internal Advisory committees- Clinical and Translational Science Awards (CTSA), Neuro-Interventional, Cerebrovascular Surgery, Emergency Medicine/Emergency Medical Services (EM/EMS), Physical Medicine and Rehabilitation /Physical Therapy(PM&R/PT), Neuro-critical Care, Telemedicine, Minority Recruitment, Pediatric Stroke, Biomarkers and Preclinical Science.
    a. Membership- Membership in these committees will be populated by investigators of the RCCs and recognized content experts appointed by the NCC. Members for each Internal Advisory Committee will rotate on a three-year basis.
    b. Responsibilities- Content specific expertise, support and feedback during the protocol review phase
    c. Meetings and Teleconference Frequency- On an as needed basis

H. External Advisory Committee-Advises the StrokeNet Executive Committee (EC).
1. Membership- Selected by PI of NCC/NDMC and NINDS on an ad hoc basis.
2. Responsibilities- Provides specific expertise, support and feedback to EC.
3. Meetings and Teleconference Frequency**-** EC ad hoc members will be invited to participate as determined necessary by the NCC or NDMC PIs.

I. **NINDS/NIH Staff-** There are designated staff at NINDS to collaborate with the StrokeNet. Included roles are but are not limited to:
1. Project Scientist- responsible for substantial scientific and programmatic involvement. This person will serve as one of the StrokeNet Co-Investigators, a full member for the Executive and Steering Committees and other committees as delegated. This role will collaborate closely with the NCC and NDMC PIs.
2. Program Director- Provides normal stewardship for the program and can serve on committees as delegated or appointed.

3. Grants Management Specialists- are responsible for the negotiation, award and administration of the project and for interpretation of Grants administration policies and provisions.
4. DSMB- NIH requires oversight and monitoring of all human intervention studies to ensure the safety of participants and the validity and integrity of the data. This policy is in addition to any monitoring requirements imposed by 45 CFR Part 46, the FDA, or the NIH Guidelines for Research Involving Recombinant DNA Activities. As needed, an independent Data and Safety Monitoring Board (DSMB) will be appointed according to NINDS policy and procedures.

5. APPLICABLE REGULATIONS

45 CFR 46 Protection of Human Subjects

6. REFERENCES TO OTHER APPLICABLE SOPs

7. ATTACHMENTS AND REFERENCES

8. **DOCUMENT HISTORY**

Version	Description of Modification Justification for Modification	Completion Date	Issue Date	Effective Date
1.0	Final	3-Jun-2014	3-Jun-2014	3-Jun-2014
2.0	Revision #1-clarification of WG term limits and process for change	6-Nov-2015	6-Nov-2015	6-Nov-2015
2.1	Biannual review with minor administrative changes	31-Oct-2016		
3.0	Final	19-Dec-2016	19-Dec-2016	19-Dec-2016

NIH StrokeNet Network

Standard Operating Procedure (SOP)

StrokeNet Organization and Governance

Version 1

ADM #17

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6/3/14

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