SOP Number: ADM 11
SOP NAME: CIRB Reliance and Approvals
Effective Date: 3-Jun-2014 (rev 12-Jan-2023)

1. POLICY

The purpose of this Standard Operating Procedure (SOP) is to define the process for an institution engaged in NIH StrokeNet affiliated research to transfer human subjects review to either the University of Cincinnati Institutional Review Board (IRB) or Advarra IRB as the Central IRB (CIRB) for NIH StrokeNet affiliated research. This SOP provides an overview of the protocol review process throughout the lifecycle of the protocol, agreed to by the Institution and the CIRB through an IRB Authorization Agreement (IAA), Reliance Agreement (RA), or other agreement by which the institution indicates that the institute cedes study oversite to the CIRB.

2. ABBREVIATIONS AND DEFINITIONS Abbreviations:

CFR	Code of Federal Regulations
CIRB	Central Institutional Review Board
CIRBI	Research Administration Portal for the Advarra IRB
CR	Continuing Review
DSMB	Data Safety Monitoring Board
fCOI	Financial Conflict of Interest
FDA	US Food and Drug Administration
FWA	Federal Wide Assurance
HIPAA	Health Insurance Portability and Accountability Act
HRPP	Human Research Protection Program
ICD	Informed Consent Document
IAA	Individual Authorization Agreement
IRB	Institutional Review Board
NDMC	National Data Coordinating Center at Medical University of South Carolina
NCC	National Coordinating Center at the University of Cincinnati
NIH	National Institutes of Health
NINDS	National Institute of Neurological Disorders and Stroke

OHRP	U.S. DHHS Office for Human Research Protections
PI	Principal Investigator
PPI	Protocol Principal Investigator
PS	Performance Site
RA	Reliance Agreement
RCC	Regional Coordinating Centers
RCS	Regulatory Compliance Specialist
RI	Relying Institution
SOP	Standard Operating Procedure
SS	Satellite Site
UC HRPP	University of Cincinnati Human Research Protection Program

Definitions:

Central Institutional Review Board (CIRB): A single Institutional Review Board (IRB) that performs the required human subjects review under the Federal Policy for the Protection of Human Subjects and other applicable regulations as deemed necessary for a multicenter trial. The NIH StrokeNet CIRB and the Advarra IRB are the CIRBs of record for StrokeNet trials.

Relying Institution (RI): An entity engaged in StrokeNet research and that has contractually agreed to rely upon the review of the StrokeNet CIRB.

National Coordinating Center (NCC): An institution designed and directly funded by NIH/NINDS to provide leadership for the StrokeNet on a national level.

NCC Project Manager: The individual responsible for being the interface with CIRB liaison and the prime award/performance sites participating in a specific StrokeNet protocol regarding approvals and modifications for protocol and local site submissions, VA CIRB approvals, annual renewals, and reportable events.

NCC Regulatory Specialist: NCC representative for network trials to interact with Performance Sites, the trial Project Manager, National Data Management Center and CIRB staff to facilitate review and preparation of documents for protocol compliance for CIRB submission and other protocol related regulatory issues. Works with the CIRB Liaison to notify the Liaison when consultation with a site is needed to understand the CIRB process and requirements if the site

needs assistance beyond the scope of the Regulatory Specialist.

National Data Management Center (NDMC): An **i**nstitution designed and directly funded by NIH/NINDS to oversee all aspects of data collection and management as well as full statistical support for StrokeNet research protocols.

Performance Site (PS): A site at which the study protocol is performed. This can be either a StrokeNet RCC Site or RCC Satellite Site or a Clinical Performance Site.

Performance Site Principal Investigator (PS-PI): Investigator who is responsible for overseeing performance of the study protocol at the performance site.

Protocol Principal Investigator (PPI): Investigator at the prime award site who is responsible for the development of the protocol and the coordination of the conduct of the clinical investigation at multiple sites, including required regulatory reporting to the CIRB, is engaged in research. If this person is the IND or IDE holder, this individual is also responsible for all applicable FDA regulatory requirements, which includes all Sponsor-Investigator responsibilities.

Prime Award Site: The institution that was awarded the grant from NIH/NINDS to oversee the study protocol.

Regional Coordinating Center (RCC): An institution designated and directly funded by the NIH/NINDS to provide leadership for the StrokeNet on a regional level over their regional Satellites and Satellite PS.

StrokeNet: NIH Stroke Trials Network

Study Protocol: The "protocol" is the written detailed description of the research project. It includes a model informed consent document and any other forms needed by the CIRB, as determined on a trial-by-trial basis.

3. SCOPE

A. The policies and procedures described in this SOP apply to parties involved with StrokeNet research, including the NCC, CIRB, NDMC and all StrokeNet RCCs, Satellites and Performance Sites.

4. PROCEDURES

A. Executing Reliance Agreements

When a site has been selected to be in a StrokeNet trial, an agreement is required that indicates the institution engaged in StrokeNet research will cede study oversite authority to the CIRB. This agreement can be referred to as a waiver of IRB oversight, an IRB authorization agreement (IAA), or a reliance agreement (RA). These agreements outline the delegation of duties between the relying institution (RI), the CIRB, and the responsibilities of each party for StrokeNet research. As the CIRB reviews StrokeNet human subjects' research,

any institution engaged in StrokeNet research should either have one of the above listed agreements directly with the CIRB or fall under the terms of an RCC's or Satellite's agreements.

Either the University of Cincinnati Human Research Protection Program (UC HRPP) Office or the Advarra IRB prepares the RA and sends it to the holder of the FWA (RI) for signature. Neither FDA nor OHRP identifies a specific signatory. Institutions may designate the FWA signatory official, the director of the human research protection program, the vice president for research, or other designees as authorized entities, in accordance with internal policies.

Fully executed agreements are returned to the RI by UC HRPP or Advarra IRB and are maintained at that institution via electronic file for institutional compliance.

Relying institutions are responsible for notifying the CIRB if their FWA is renewed, revised, restricted, suspended, or terminated while the reliance agreement is in effect.

B. Protocol Review Startup for the CIRB

1. Prime Award Protocol Approval

Prime Award Protocol Startup Packets for CIRB review will include but are not limited to the following:

a. PPI CV
b. CIRB financial Conflict of Interest forms (fCOI)
c. Trial specific StrokeNet CIRB Assurance Statement (Attachment A – UC IRB only)
d. Protocol
e. Template ICD to be used by PS
f. Prime Award Application Form (UC IRB only)
g. FDA Approval Letter or relevant correspondence (IND, IDE)
h. FDA 1572 & 3455
i. Investigator Brochure/Package Insert/Instructions for Use (study protocol specific documents)
j. Recruitment materials

2. Performance Site Approval Startup packets for performance site approval will include but are not limited to the following:

a. Trial specific CIRB financial Conflict of Interest forms (fCOI)
b. Trial specific StrokeNet CIRB Assurance Statement (Attachment A – UC IRB only)
c. Protocol (version approved by the CIRB for the PS Regulatory files)
d. Protocol CIRB Approval Letter (version approved by the CIRB for the PS Regulatory files)
e. Protocol Signature Page
f. Template ICD (approved by the CIRB for use with the protocol) with instructions for performance site local modifications to "modifiable sections" – Clean and Tracked Changes copies need to be submitted once site has completed their local modifications
g. Trial specific Local Site Context and IRB/HSP Review Form (Attachment B – StrokeNet

CIRB only)
h. Protocol Specific StrokeNet Performance Site Application Form – StrokeNet CIRB only)
i. Wavier of HIPAA Authorization Request for screening purposes
j. FDA 1572 & 3455
k. PS-PI CV
l. Site specific recruitment materials

C. CIRB Review and Approval of the Prime Award Protocol

1. PPI will send complete and accurate startup package to the NCC Administrative Co-Director or NCC Project Manager for review and submission to CIRB. The PPI will respond to CIRB related queries sent by the NCC to facilitate CIRB review.
2. NCC Administrative Co-Director or Project Manager facilitates communication with PPI and prime award protocol team during the startup process for regulatory guidance. They act as the liaison to return CIRB approved documents to the PPI for the regulatory files and notifies the PPI that PS can begin their submission process.
3. The CIRB reviews the study protocol for the Prime Award. The CIRB approves performance sites after the CIRB approves the study protocol for the Prime Award.

D. CIRB Review and Approval of Performance Sites

1. PS-PI will coordinate relevant local ancillary reviews as required by local policies in conjunction with the local HRPP Office/IRB/General Council. They then complete the local context via CIRB specific instruction. The PS will customize the approved study-protocol template ICD, only in the areas permitted to include/reflect information specific to the PS then negotiate any other additional changes to the ICD with NCC Project Manager or Regulatory Specialists prior to CIRB submission. The PS may also provide any requests for partial waivers to be reviewed by the CIRB acting as the Privacy Board at this time (this includes partial HIPAA Authorization Waiver for screening).
2. The CIRB will review and approve PS submissions. NCC Project Manager or Regulatory Specialists will provide the PS their approved study documents and instructions for site activation next steps.

E. Continuing Review

1. The expiration date for continuing review will be set by the review date of the study protocol. Prior to this expiration date, the NCC Project Manager will send out a reminder and instructions to all PS along with the NDMC and a request for information to support the CIRB Continuing Review.
2. The PS will submit requested continuing review information as specified by the NCC Project Manager or the IRB of record.
3. The NDMC will prepare the CIRB Continuing Review Report with data tables for enrollment and study completion, along with demographics for the study- wide report and each PS (StrokeNet CIRB only). They will also provide a copy of the DSMB reports or if there is not a DSMB will report provide a listing of protocol deviations.
4. The PPI will compose study wide continuing review updates and return it to the NCC Project Manager for CIRB submission.
5. The CIRB will review the continuing review submissions and provide approval letters and

next review date.

6. After CIRB approval of Continuing Review, NCC Project Manager and/or Regulatory Specialist will distribute documents to the PS for upload into WebDCU for NCC review and approval.

F. Modifications

Throughout the course of a StrokeNet trial, any changes to the protocol will be considered and processed as modifications. Modifications will be generated in two ways: 1) the PPI may initiate a change to the prime-award protocol or study materials; or 2) a PS-PI may initiate an administrative modification (changes in site personnel or facilities). Recruitment materials not submitted with the original submission of the prime award protocol or PS may also be submitted to the CIRB as an administrative modification.

G. Reportable Events

For reporting of non-compliance, subject injuries, unanticipated problems, protocol deviations/violations, complaints, cessation/suspension/termination of protocol, changes made without CIRB approval to eliminate apparent immediate hazards to subject(s) and other required reports, see the StrokeNet Reporting SOP ADM 13.

H. Study Closure

1. **Protocol Closure**
   Responsibilities follow those outlined within the CR section.
2. **Performance Site Closure Prior to Study Completion**
   If the site is closing at a time point earlier than the Protocol, the site will need to coordinate the reporting of the site's enrollment and study completion table from the NDMC through the NCC Project Manager. The NCC Project Manager or performance site submits the closure to the CIRB. The CIRB conducts the office review and creates the acknowledgment documents.

5. APPLICABLE REGULATIONS

45 CFR 46.114
21 CFR 56.114

6. REFERENCES TO OTHER APPLICABLE SOPs

ADM 2 Conflict of Interest and Financial Disclosure Requirements
SOP ADM 12 CIRB Reporting SOP

7. ATTACHMENTS

A. StrokeNet CIRB Assurance Statement
B. Local Site Context and IRB/HSP Review Form (model template)
C. StrokeNet CIRB Procedures for Conducting the Informed Consent Process With Individuals That Do Not Understand English or Have Low Literacy Skills
D. StrokeNet Translation Policy

8. LINKS

https://research.uc.edu/support/offices

9. 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
1.1	Biannual Review with administrative changes	14-Sep-2016		
2.0	Final	1-Feb-2017	1-Feb-2017	1-Feb-2017
3.0	Revised with new FWA verification procedure, NCC Regulatory Specialist added	4-Sep-2018	4-Sep-18	4-Sep-18
3.1	Minor administrative changes, updated attachments	1-Mar-2020	1-Mar-2020	1-Mar-2020
4.0	Generalization and summarization of CIRB processes	12-Jan-2023	2-Feb-2023	2-Feb-2023

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NIH StrokeNet Network

Standard Operating Procedure (SOP)

Central Institutional Review Board (CIRB) Reliance

Version 2

February 2017

ADM #11

Originators: NIH StrokeNet NCC Personnel

Reviewed and Approvedby: