SOP Number: ADM 02
SOP NAME: Reporting Conflict of Interest and Financial Disclosures
Effective Date: 1-September-2019

1. PURPOSE

NIH StrokeNet (StrokeNet) investigators and staff at multiple institutions who participate in the network or a StrokeNet managed trial may receive both federal and industry funding. There is also the potential for a close association with the therapeutic products used to treat acute stroke "that ... while not intrinsically unacceptable, [may] raise the prospect that scientific advances will bring financial gain for the research scientist and his or her institution." (Conflict of Interest Workshop Executive Summary, National Institutes of Health (NIH), Bethesda MD September 30, 2002). As such, the potential for conflicts of interest (COI), of any kind and degree, is considerable. Documenting and maintaining records regarding the objectivity of investigators and administrative trial staff present a considerable challenge for the institutions involved, as well as the National Coordinating Center (NCC), but is a challenge that must be addressed both ethically and practically. Hence, the purpose of this SOP is to document the process by which the StrokeNet will assure compliance for trials managed under the network with Department of Health and Human Services (DHHS) financial Conflict of Interest (FCOI) regulatory requirements, including those of the National Institutes of Health (NIH) and the Food and Drug Administration (FDA).

2. DEFINITIONS AND ACRONYMS

Awardee Institution who receives the prime award from the respective NIH agency (also known as Prime Awardee)

cIRB StrokeNet Central Institutional Review Board at the University of Cincinnati

COI Conflict of Interest

DHHS Department of Health and Human Services

FID Financial Interest Disclosure

FDA Food and Drug Administration

FCOI Financial Conflict of Interest

MTA Master Trial Agreement

NCC National Coordinating Center on behalf of the University of Cincinnati

NDMC National Data Management Center at Medical University of South Carolina

NIH National Institutes of Health

NINDS National Institute of Neurological Disorders and Stroke

Non-StrokeNet Protocol Awarded Performance Site Institutions operating within StrokeNet on behalf of specific protocols that are not RCCs nor are affiliated with RCCs

PHS Public Health Service

PI Principal Investigator

Policy An overall plan to guide and determine present and future decisions

Procedures Established or prescribed methods to be followed routinely

PTE Pass-through entity (also known as National Coordinating Center)

CTA	Clinical Trial Agreement
RCC	Twenty-five Regional Coordinating Centers with a NINDS NIH StrokeNet. The RCC has executed a MTA and a cIRB Reliance Agreement or external IRB reliance with the NCC to participate in StrokeNet trials/activities.
RCC PS	Performance site - an entity that has agreed with the RCC to serve as a clinical trial performance site for StrokeNet affiliated studies. The PS functions under the direct leadership of the RCC.
SS	Satellites site - an entity named by an RCC as part of its regional network. A SS may or may not be a performance site for a clinical trial for StrokeNet affiliated studies. The SS has executed a MTA and a cIRB Reliance Agreement with the NCC to participate in StrokeNet trials/activities.
SS PS	A SS may have multiple SS performance sites that may serve as a clinical trial performance site for StrokeNet affiliated studies.
SOP	Standard Operating Procedure
StrokeNet	NIH StrokeNet Network
Sub-I	Sub-investigator

3. SCOPE

This SOP applies to all personnel involved with the StrokeNet - investigators, staff, subcontractors, consultants or other entities associated with the StrokeNet who manage, oversee, and conduct research within the network regulated by the Public Health Service (PHS) and/or the FDA. This SOP is applicable to the NCC, the NDMC, the RCC, SS and PS, and all non-network protocol awarded centers.

4. STROKENET COI REPORTING POLICIES AND PROCEDURES

A. Who must complete financial interest disclosure (FID) and financial Conflict of Interest (FCOI) information?

There are three pertinent but different definitions of investigators used in specific reporting requirements. The term investigator is used in this SOP to define who is required to submit FID and FCOI.

1. DHHS/PHS/NIH Definition of Investigator (42 CFR Part 50 Subpart F) - Definition of Investigator - Investigators are defined as the "project director or principal investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, which may include, for example, collaborators or consultants" (42 CFR Part 50.603).

2. StrokeNet Central IRB (cIRB) Definition of Investigator - listed or identified investigator who is directly involved in the treatment or evaluation of research subjects for a specific trial. The term also includes the spouse and each dependent child of the investigator. The cIRB reviews these documents to determine if any outside activities disclosed could be related to the

protocol (appearance or actuality) and will determine appropriate safeguards to protect the rights and well-being of human subjects.

3. FDA Regulation (21 CFR Part 54) - All investigators in any sponsored clinical research that will be used in part to support a marketing application for a human drug, biological product, or device must submit conflict of interest disclosures on a specified FDA form (1572), including any financial interest of the investigator in the product and a statement of any compensation for the investigator that could be higher for a favorable outcome of the clinical study than for an unfavorable outcome.

B. Who has the responsibility for Reporting FCOI for DHHS/NIH/PHS funding In NIH StrokeNet?

As stipulated in NIH/NINDS notice of grant awards, all recipients *must* promote objectivity in research by establishing standards that provide reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's FCOI in accordance with the cited regulations.

42 CFR Part 50.604 requires that institutions conducting PHS-funded research "Maintain an up-to-date, written, enforced policy on financial conflicts of interest." Further, "If the Institution (Awardee) carries out the PHS-funded research through a subrecipient (e.g., subrecipient site, subcontractors or consortium members), the Awardee (Prime Awardee) must take reasonable steps to ensure that any subrecipients (sites) Investigator complies with this subpart by incorporating as part of a written agreement with the subrecipient sites terms that establish whether the COI policy of the Awardee (Prime Awardee) institution or that of the subrecipient (site) will apply to the subrecipient's Investigators."

Importantly, while the NCC (or PTE) will help administer and review CTA documents to identify which subrecipients sites indicate: (a) that they follow the Prime Awardee COI policy or (b) follow their own PHS-compliant COI policy (in accordance with 42 CFR Part 50 Subpart F, 50.604 (C)), the NCC (or PTE) will not be responsible for FCOI administration and/or compliance on behalf of the Prime Awardee, unless agreed to by the NCC and articulated in the subaward issued by the Prime Awardee to the NCC at the University of Cincinnati. **See attachment B for guidance.**

5. SUBRECIPIENT SITES

A. Documentation and for FCOI administration and compliance for subaward sites. The NIH StrokeNet MTA and CTA documents contain the following language to identify whether the Awardee institution will be responsible for a subrecipient's (site's) compliance or if the subrecipient (site) indicates that they have a PHS-compliant COI policy.

Each Subrecipient site must designate herein whether the COI policy of the (check one)
___ Awardee institution (Prime Awardee), or
___ Subrecipient (site) will apply (not PTE or NCC).

If applying its own financial conflicts of interest policy, by execution of this Subaward Agreement, Subrecipient site certifies that its policy complies with 42 CFR Part 50 Subpart F.

Subrecipients complying with the awardee institution's (Prime Awardee's) financial conflict of interest policy are required to complete the following four items prior to issuance of a subaward:

1) All individuals considered investigators must complete the Prime Awardee's disclosure form (paper or online);
2) Investigators must receive and review the awardee (Prime Awardee) institution's Conflict of Interest (COI) Training;
3) Investigators must receive and review the awardee (Prime Awardee) institution's Conflict of Interest Policy; and
4) Investigators must certify that they have received and understand the awardee (Prime Awardee) institution's Conflict of Interest Policy and COI Training, completed their disclosure honestly, and agree to update their FID within 30 days of any changes.

For sites wanting to use the awardee (Prime Awardee) institution's policy: Investigators are defined as the "project director or principal investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, which may include, for example, collaborators or consultants" (42 CFR Part 50.603).

The NCC will review and verify that subrecipient sites who claim to have a PHS-compliant policy are listed on the FDP Clearinghouse or FDP Expanded Clearinghouse list. If the subrecipient site is not listed on one of the Clearinghouses, the NCC will notify the Awardee (Prime Awardee) and it will be the responsibility of the Prime Awardee to follow up with subrecipient sites to determine next steps for compliance **(See Attachment B)**.

B. Subrecipients: What is required to be reported to the NCC or Awardee for compliance with PHS COI regulations (42 CFR Part 50 Subpart (50.604 (c))?

Subrecipients following the Awardee's PHS-compliant COI policy.
A subrecipient site shall follow the Prime Awardee's policy in accordance with 42 CFR Part 50 Subpart F in terms of disclosure requirements, policy review, and training. Any FCOI related to the research will be reviewed and managed by the Prime Awardee. The Prime Awardee will report identified FCOI to the NIH via eRA Commons. Such report shall be made prior to expenditure of funds authorized in the CTA and within 60 days of any subsequently identified FCOI.

Subrecipients following their own PHS-compliant Policy.
For subrecipient sites who are complying with their own PHS-compliant COI policy, any identified financial conflicts of interest (FCOI) related to a StrokeNet clinical trial must be reported to trial-specific NCC Project Managers. The NCC will contact the Prime Awardee who has the responsibility under the NIH award to report the FCOI directly to the NIH via eRA Commons. Such report shall be made before expenditure of funds authorized in the Clinical Trial Agreement and within 60 days of any subsequently identified FCOI.

6. TRIAL SPECIFIC FCOI REPORTED to cIRB (when University of Cincinnati serves as the cIRB)?

A. What trial specific FCOI must be reported to the cIRB when University of Cincinnati serves as the IRB of record (cIRB)? A Trial Specific FID form must be completed by any Protocol or Performance Site Principal Investigators (PI) when the NCC is the cIRB of record.

1. A Trial Specific FID form (attachment A) will be used to identify any "company" or other entity that contributes in some way to the support of the trial. The FID form will be distributed by the Project Manager to the trial performance sites. The StrokeNet cIRB will use the criteria on the form to identify the PI's financial interest(s). If the PI indicates having any of the interests listed on the form, a separate explanation (including the amount of compensation received in the previous twelve months) is requested from the PI on the FID form. The cIRB will use this explanation to determine the presence of a trial specific FCOI. If there is a trial specific FCOI, the significance of any trial specific FCOI will also be assessed. All information provided will be treated as confidential to the extent permitted by law.

2. Trial specific investigator FCOIs identified by the relying institutions for any other study investigators.
Investigators are defined as the "project director or principal investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, which may include, for example, collaborators or consultants" (42 CFR Part 50.603)

B. Trial Specific Principal Investigator's FCOI cIRB Review Procedures:

1. The trial Specific PI FID forms will be initially received and screened by the StrokeNet Project Manager and cIRB Liaison. Refiling will occur at annual intervals, within 30 days of a change and at the end of the trial.
2. If a financial interest is indicated, the StrokeNet cIRB liaison will contact the PI to identify the particular circumstances of the interest and request a written explanation to determine the individual's role in the trial and the exact nature and extent of the interest if one was not provided.
3. If the PI's StrokeNet FID form indicates a reportable FCOI per PHS regulations, the cIRB Liaison will contact the NCC (University of Cincinnati) COI officer who may execute a "public accessibility" request to the PI's home Institution.
4. All information collected will be kept confidential and submitted only to cIRB for evaluation. If deemed necessary, the cIRB will request the PI's institutional COI office to assist in the development of a protocol specific management plan for the reported FCOI. In these instances, the NCC COI officer will work closely with the PI's institution (COI office) to understand the terms of the management plan and to implement them accordingly. If the subrecipient

institution has its own COI policy in compliance with 42 CFR Part 50, the cIRB defers to the investigator's institutional policy to identify and manage conflicts of interest; however, the cIRB may add additional protocol-specific safeguards to protect the welfare of subjects and the integrity of the research where appropriate.

5. A copy of the protocol specific COI management plan will be archived with the cIRB regulatory files and a copy will be submitted to the PIs Institution's COI Office. The PI's Institution can add to the individual's cIRB management plan but cannot remove any stipulations.

C. Trial Specific Investigator FCOI cIRB Review Procedures:

1. The relying (subrecipient) institution will provide a description of the FCOI and the management for the FCOI.
2. The trial Specific FCOI and management will be initially received and screened by the StrokeNet Project Manager and cIRB Liaison.
3. The cIRB liaison will provide the information to the NCC COI officer.
4. The NCC COI officer will work closely with the relying (subrecipient site) institution's COI office to understand the terms of the management plan and to implement them accordingly.
5. The cIRB defers to the investigator's institutional policy to identify and manage conflicts of interest; however, the cIRB may add additional protocol-specific safeguards to protect the welfare of subjects and the integrity of the research where appropriate.

CI. When will PI Trial Specific FCOI information need to be updated?

1. If new drugs or devices are added to an existing cIRB reviewed protocol or an industry sponsor of a study changes, the FID form will be updated accordingly. PIs will be required to sign and submit the updated form.
2. If existing products are acquired through a merger or purchased by a new corporate entity, PIs may be required to sign a new FID form. Every attempt will be made to remain current, but changes in corporate status can occur without notification.
3. PIs are expected to notify the cIRB within 30 days of any change in their status and submit the appropriate updated form.
4. Relying Institutions must report any newly identified investigator FCOIs to the cIRB within 30 days.

CII. Document Management and Retention for StrokeNet cIRB

1. All completed FID certification forms, explanations of disclosure documents, public accessibility reports, and cIRB management plans will be stored in a secure manner (for example, under lock and key or a stand-alone computer with no internet/network access) for the life of the network plus five (5) years. After that time this record maybe destroyed. More specifically, all FCOI statements will be blinded for the investigators name only; center/site affiliation will remain

intact. The blinded FCOI- forms will be scanned and stored on electronic storage medium for the life of the network plus five (5) years.

2. The NIH StrokeNet Clinical Performance Sites are required to collect a StrokeNet FCOI form initially for all study team members and any new investigator on a trial. Sites are to file the forms onsite (electronically or as paper files) for all study team members and made available for monitors/auditors when requested for the length of the trial. Sites are to refer to their local policy/requirement for annual renewal of the FCOI during the continuing review process. Sites will be asked to verify that there have not been changes to any study team member's FCOI on the continuing review form submitted to the cIRB annually. Key study personnel should always disclose any FCOI as soon as it is presented so that it can be collected and submitted to the cIRB. Study team members' disclosures will be stored in WebDCU™ along with the site PI FID form in the designated site section.

F. When external/commercial IRB (e.g., Advarra) is the IRB of Record for StrokeNet protocols

1. When an external IRB is the IRB of record for a StrokeNet protocol, the external IRB will follow regulations governing conflicts of interest as stipulated in 45 CFR Part 46 which directly addresses conflicts of interest by requiring that "no IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB" (45 CFR 46.107(e)).

2. **Prime Awardee's responsibilities**
Commercial/external IRB (e.g., Advarra) does not comply with PHS regulations on "Objectivity in Research" per PHS regulations 42 CFR Part 50 Subpart F. Instead, trial-specific NCC Project Managers will help review if subrecipient sites have PHS-compliant policies upon completion of the CTA and will notify the Prime Awardee of those who indicate that they need to follow Prime Awardee's COI policy or for subrecipient sites who indicate a PHS compliant COI policy but whose site is not found under the FDP Clearinghouse or FDP Clearinghouse Expanded Entity list. The Prime Awardee will need to reach out to these sites to obtain their COI policy to determine compliance with 42 CFR Part 50 Subpart F. The NCC will provide the Prime Awardee with a list of these potential noncompliant subrecipient sites as well as points of contact for purposes of reaching out to obtain the respective entity's COI policy. For subrecipient sites who have a compliant policy, they can follow their own policy, and this will be noted accordingly on the CTA. For subrecipient sites who do not have a compliant COI policy, those sites will need to follow that of the Prime Awardee's COI policy **(not NCC or PTE)** in terms of policy, training, disclosure, and notification of any FCOI. **See Attachment B for additional information.**

7. REVIEW OF COI STATEMENTS BY StrokeNet LEADERSHIP

The PI of the NCC is consulted on certain but not all cases of investigator/staff FCOI. The cIRB will share the final results of its review with the applicable PI as deemed necessary and with the RCC PI if the NCC PI makes the request.

8. PUBLICATION AND/OR PUBLIC ACCESS TO StrokeNet FCOI FORMS

Procedure for Access to Network FCOI Statements:

1. Permission to review FCOI statements for StrokeNet must be made in writing to the StrokeNet PI. The purpose of the review of this information must be clearly documented, signed, and dated by the requestor.
2. The decision to grant permission to view unblinded and later blinded FCOI will be made by majority vote of the Executive Committee (EC). If the EC has disbanded, the responsibility to grant this permission will rest with the StrokeNet NCC PI alone.

9. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 54	Financial Disclosure by Clinical Investigators
21 CFR 812.43	Selecting Investigators and Monitors
21 CFR 312.53	Selecting Investigators and Monitors
42 CFR 50 Subpart F	Promoting Objectivity in Research
2 CFR 200	Uniform Administrative Requirements, Cost Principles, And Audit Requirements For Federal Awards
45 CFR 94	Responsible Prospective Contractors

FDA Guidance, Compliance & Regulatory Information (Drugs)
https://www.fda.gov/Drugs/GuidancecomplianceRegulatoryInformation/Guidances/default.htm

FDA Standards and Guidances for Neurological Devices
https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/NeurologicalDevices/ucm528789.htm

10. REFERENCES TO OTHER APPLICABLE SOPS

11. ATTACHMENTS AND REFERENCES

A. FCOI form
B. Prime Awardee and Subrecipient Process

11. DOCUMENT HISTORY

Version	Description of Modification	Completion Date	Issue Date	Effective Date
1.0	Final	3-Jun-2014	3-Jun-2014	3-Jun-2014
2.0	May 2017 Revision Final	11-Apr-2017	26-May-2017	26-May-2017
3.0	Revise trial specific FCOI process	22-Aug-2019	22-Aug-19	1-Sept-2019
4.0	Address external IRB COI process and Prime Awardee responsibilities	12-May-2022	20-Jun-2022	20-Jun-2022

Attachment A

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

FINANCIAL CONFLICT OF INTEREST FORM

Please complete and return with any protocol submitted for initial and continuing review.

Study Title:

Study Sponsor Name:

For purposes of completing this form, a Sponsor is a party supporting a particular study at the time it was carried out. Typically, a trial is either an industry sponsored or investigator sponsored trial (if funded by a grant or award). If you are uncertain which to indicate consult the NCC CIRB liaison before submitting this form.

Name of Site PI: _____

Name of Person Completing Form: _____

Your Role in Study:_____

(for example, Investigator, Study Coordinator, Statistician, Research Nurse, data entry)

A "financial interest related to research "means a financial interest in the sponsor, product or service being tested. In order to protect participants from financial conflicts of interest the IRB requires that such potential conflicts during the past 12 months be disclosed. If the IRB determines that a conflict exists that could influence the research or jeopardize the well-being of participants, the IRB may require additional information about the conflict or may require that the conflict be resolved before the research is approved. In addition, it may require that the conflict be disclosed to the participant in the Informed Consent Statement.

Please indicate the following:

☐ Yes ☐ No I or a member of my immediate family own(s) equity (stock ownership, stock options, convertible note(s), or other ownership interest in any amount) in the company or other legal entity whose drug, procedure, technique, device, or

software I am testing (the "Company").

☐ Yes	☐ No	The Company holds patent rights to inventions created by me or a member of my immediate family (spouse, children, parent, in-laws, and siblings).
☐ Yes	☐ No	I or a member of my immediate family hold(s) a position of senior management officer, or director of the Company.
☐ Yes	☐ No	I or a member of my immediate family am/is a scientific advisor, consultant, or speaker for the Company and receive payments from the Company (including direct or indirect payments, honoraria, and all other forms of compensation).
☐ Yes	☐ No	If a device, technique, software, or procedure involved in the research is marketed, I or a member of my immediate family may be entitled to royalty income or income from the sale of the product.
☐ Yes	☐ No	I or a member of my immediate family have/has a financial interest that may appear to conflict with the protection of subjects or which should be disclosed to subjects in order to secure informed consent.

IF ANY BOX ABOVE IS CHECKED YES, INCLUDE ON A SEPARATE SHEET AN EXPLANATION OF THE CONFLICT (INCLUDING THE AMOUNT OF MONEY) FOR THE IRB'S CONSIDERATION. INFORMATION PROVIDED IS CONSIDERED CONFIDENTIAL.

My signature below is my representation that I have accurately completed this form to the best of my knowledge.

Signature	Date

If the investigator is disclosing a financial interest (i.e. checked "YES" in one of the boxes on the fCOI form), please provide the following information:

1. Identify the entity(s) of which the investigator has a financial relationship.

2. What is the amount of compensation received from that entity(s) in the past 12 months?

3. What is the amount of compensation expected from that entity(s) in the coming 12 months?

4. Please provide a description of the kind of service(s) provided to that entity(s) (e.g., consulting, speaking, proctoring, etc.)

5. Has your institution reviewed this financial disclosure in relation to the StrokeNet protocol?
   YES ☐ NO☐

   a. If yes, has your institution identified this as a conflict of interest requiring management?
      YES ☐ NO☐

   OR

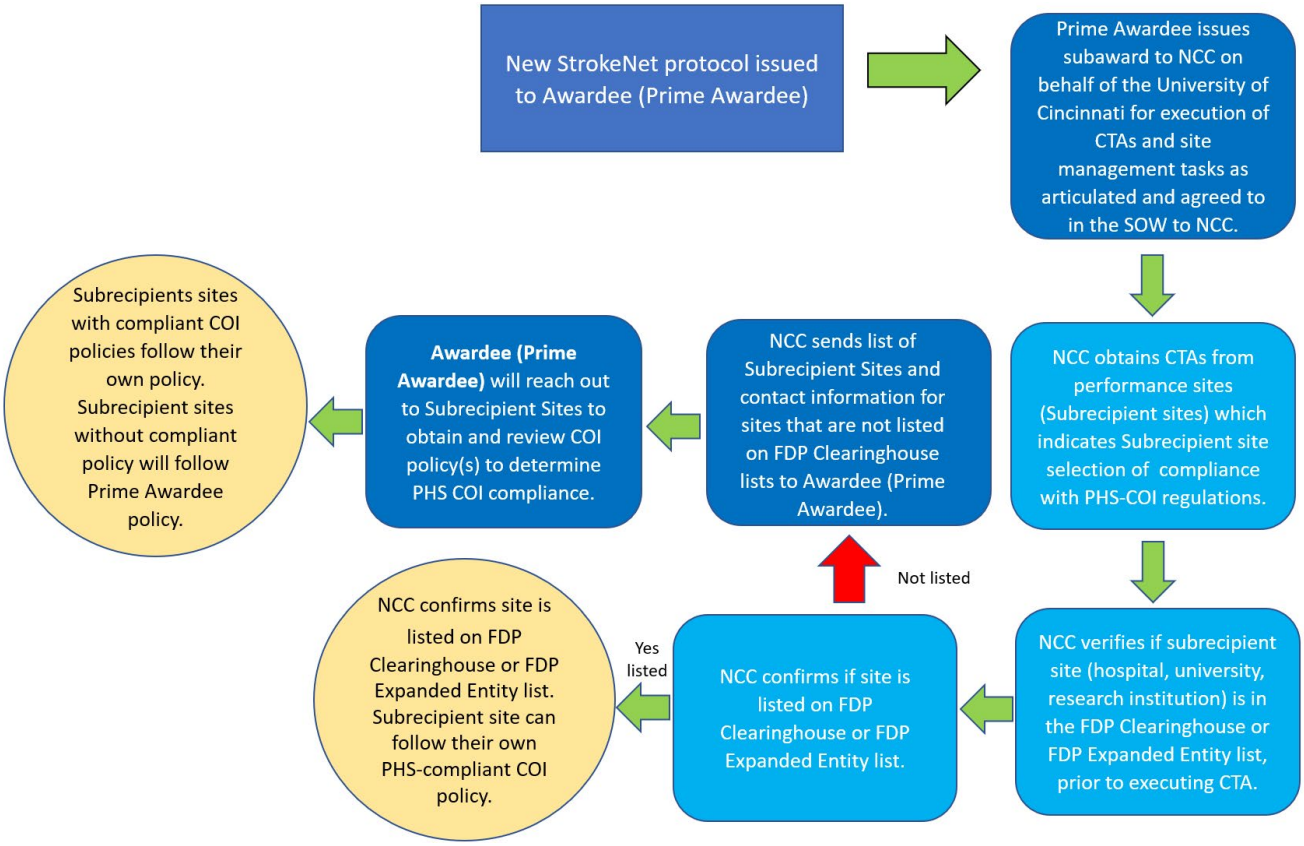
   Did your institution review it and deem it not to be a conflict?

   YES ☐ NO☐

   b. If yes, please provide the conditions/stipulations of how your institution is managing the conflict (e.g., disclosure in informed consent, change in research role/responsibilities, etc.)

Signature	Date

Attachment B



NIH StrokeNet Network

Standard Operating Procedure (SOP)

Reporting Conflict of Interest

And

Financial Disclosures

Version **v4.0**

ADM #02

Originators: StrokeNet National Coordinating Center Personnel

Reviewed and Approved by:

(Date) 6/10/2022

Pooja Khatri, MD (StrokeNet NCC MPI)

Lawrence S. Janis -S

Digitally signed by Lawrence S. Janis -S
Date: 2022.06.21 09:30:54 -04'00'

_____ (Date) _____

Scott Janis PhD (NIH/NINDS Representative)

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