SOP Number: GCP 03
SOP NAME: Informed Consent and NIH StrokeNet Trials
Effective Date: 22-Dec-2015

1. Policy

The purpose of this Standard Operating Procedure (SOP) is to describe the requirements for obtaining informed consent and documenting the process for all NIH StrokeNet research subjects. Informed consent is an ethical requirement for conducting research with human subjects, and refers to the ongoing process of providing detailed information about the study to potential and continuing research subjects. Informed consent at NIH StrokeNet Clinical Trial Performance Site (CTPS) will be conducted in accordance with federal and state regulations and Good Clinical Practices (GCP), as set forth in the 1996 ICH E6 Consolidated Guidance.

2. Abbreviations

CTPS	Clinical Trial Performance Site
NCC	National Coordinating Center - located at the University of Cincinnati
NDMC	National Data Management Center – located at Medical University of South Carolina
CIRB	Central Institutional Review Board
ICF	Informed Consent Form
GCP	Good Clinical Practice
SOP	Standard Operating Procedure

3. Definitions

Assent	An affirmative agreement by a child (see below) to participate in a clinical investigation.
Child	A person who has not attained the legal age of consent for treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted.
Exculpatory Language	Language (either verbal or written) through which the potential subject or representative is made to waive or appear to waive any of the subject's legal rights or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Family Member	Any one of the following legally competent persons: spouse; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.
Guardian	An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research.
Illiterate	A person who is unable to read or write.
Legally Authorized Representative	An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in clinical research.
Parent	A child's biological or adoptive parent.
Surrogate	A family member or friend who is authorized to act on behalf of the subject.
Ward	A child who is placed in the legal custody of the State or other agency, institution or entity, consistent with applicable federal, state or local law.
Consent Capacity	An adult's ability to understand information relevant to making an informed, voluntary decision to participate in research.

4. Scope

This SOP applies to any individual involved in enrolling subjects or planning for enrollment of subjects for a NIH StrokeNet clinical study. The scope of this SOP includes all members of the CTPS research staff and, within the context of their oversight and advisory roles for the NIH StrokeNet, the National Coordinating Center (NCC) and the National Data Management Center (NDMC), as well as to all researchers, staff, subcontractors or other entities associated with the NIH StrokeNet Network. This SOP has been developed to ensure compliance with Federal regulations and Good Clinical Practice, as set forth in the 1996 ICH E6 Consolidated Guidance manual.

The NIH document titled "**Research Involving Individuals with Questionable Capacity to Consent**" (see reference) offers the following issues for consideration regarding enrolling subjects with impaired consent capacity into clinical trial. : "*In order for individuals with impaired consent capacity to be ethically enrolled in research, investigators and IRBs should consider ways to enhance subjects' understanding of information relevant to the consent process, in a manner consistent with the Common Rule and the ethical principles outlined in the*

Belmont Report. Because individuals with impaired capacity to consent may be vulnerable to coercion or undue influence, investigators and IRBs should be guided by ethical principles such as respect for persons and equitable selection of research subjects, and they should weigh the need for additional safeguards to ensure the voluntariness of study participation. In some cases, enrolling individuals with impaired consent capacity in research may necessitate the involvement of a legally authorized representative (LAR).When an LAR is acting on behalf of the prospective subject, IRBs should consider the most appropriate methods to present information to the LAR and the subject about the study and its risks and anticipated benefits."

5. Procedures

The purpose of the informed consent process is to ensure that study subjects understand the nature of the research activity through all stages of the project, and that they are voluntarily choosing whether or not to begin or continue participation in the research study. Stroke research subjects may include adults, children, non-English speaking or illiterate populations. It has been noted that neurologic disorders such as stroke or dementia can impair an adult's consent capacity. As a component of the protocol review and approval process the CIRB for the NIH StrokeNet will address this issue for each trial and require documentation denoting appropriate methods to determine decision making capacity in the targeted patient population and for the trial design.

The Consent Process

The informed consent process begins before the subject is enrolled, and continues until after the subject has completed participation in the research study. The initial informed consent process takes place before any study-related procedures are performed. The ongoing informed consent process may only be amended if Federal criteria are met and necessary approvals for emergency research or other waivers of consent are obtained.

To ensure that research subjects are fully informed prior to their participation in the research, it is important that the entire informed consent process is presented to a subject or his/her representative at a level that is appropriate to their level of education or comprehension. The information conveyed should be clear and easily understood to enable the person to make a decision whether or not to participate in the research. The individual or representative must be able to clearly understand the risks and the potential benefits (if any), and to be aware that their initial and ongoing participation is entirely voluntary.

Subjects who do not speak English should be presented with a consent document written in a language understandable to them. The process for this will be defined in part by the CIRB and the CTPS but will be consistent with those procedures as defined in 45 CFR §46.16 and §45.117.

Subjects who are younger than the age of majority in their state of residence at the time of enrollment may be offered the opportunity to provide assent, if applicable. In general, the parent/guardian would provide informed consent for the child if the child is not old enough to assent to participation in the research. If the child is able to understand the nature of participation in a study, the child may provide assent. Federal guidelines generally allow wards to be enrolled in clinical investigations only if such clinical investigations are related to their status as wards or are conducted in schools, camps, hospitals, institutions or similar settings in which a majority of children involved as subjects are not wards. However, state laws vary on this issue.

The informed consent form (ICF) will include thee basic elements as described in 21CFR 50.25. The process of informed consent will be conducted by trained, CIRB-approved study personnel. The process includes (but is not limited to) the following steps:

- presenting information about the study, including the risks and potential benefits, at a level that allows for clear understanding;
- allowing the potential subject or representative the adequate opportunity to read the ICF document;
- answering any initial questions;
- clearly stating that initial and ongoing participation in the study is voluntary, and that a subject may discontinue participation at any time;
- obtaining relevant signatures on the ICF; and
- continuing to provide information and answers to questions throughout study participation.

In the case that a potential subject is illiterate or otherwise unable to sign the ICF in the usual manner, an attempt should be made to provide an impartial third party to witness the informed consent process and to sign the ICF on behalf of the subject. The subject will be permitted to acknowledge consent in a manner consistent with state law. In the case that a potential subject is not able to provide consent, some protocols may allow the subject to be enrolled by a surrogate, if such a process is approved by the CIRB (and the local IRB, if applicable) prior to the informed consent process.

A. Documentation of Informed Consent Process

The following information will be reviewed and included when documenting the Informed Consent Process:

- Verify that the ICF is the most recently approved version
- The process that was followed prior to signing the ICF
- Date and time Informed Consent was obtained

- Who was present when the subject was consented
- Participant/family/legal representative who reviewed the ICF, if applicable
- Verification of participant/family/legal representative comprehension of the Informed Consent, if applicable
- Verification that all questions posed by the potential subject were answered by designated study staff
- Statement that ICF was signed before any study assessments or procedures were performed
- If the consent is to be signed on the same day that study procedures will be performed, document the time that the consent was signed.

6. **Applicable Regulations and Guidelines**

The Belmont Report	Ethical Principals and Guidelines for the Protection of Human Subjects of Research. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979).
21 CFR Part 50	Protection of Human Subjects
21 CFR 50.20, 23, 24, 25, 26, 27, 55, 56	Informed Consent of Human
Subjects 21 CFR 56.109	IRB Review of Research
21 CFR 312.60	General Responsibilities of Investigators
45 CFR 46.111	Criteria for IRB Approval of Research
45 CFR 46.116	General Requirements for Informed Consent
45 CFR 46.117	Documentation of Informed Consent
ICH E6	Good Clinical Practice: 1.9, 4.8.1, 4.8.3, 4.8.5, 4.8.7, 4.8.8, 4.8.9, 4.8.10, 4.8.11, 4.8.15 (http://www.fda.gov/cder/guidance/959fnl.pdf)
FDA Information Sheets	The Consent Process (http://www.fda.gov/oc/ohrt/irbs/informedconsent.html)
OHRP	Tips on Informed Consent (Revised 3/16/93) http://www.hhs.gov/ohrp/humansubjects/guidance/ictips.html
OHRP	Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English (November 9, 1995) http://www.hhs.gov/ohrp/humansubjects/guidance/ic-non- e.htm

National Institutes of Health, Office of Extramural Research	Research Involving Individuals with Questionable Capacity to Consent: Points to Consider, http://grants.nih.gov/grants/policy/questionablecapacity.htm

7. References to Other Applicable SOPs

ADM SOP 11 Central Institutional Review Board (CIRB) Reliance

8. Attachments and References

N/A

8. Document History

Version	Description of Modification	Justification for Modification	Completion Date	Issue Date	Effective Date
1.0	Final		17-Dec-2015	22-Dec-2015	4-Jan-2016