SOP Number: ADM 12
SOP NAME: The NIH StrokeNet Central Institutional Review Board (CIRB) Reporting
Effective Date: 3-Jun-2014

1. POLICY

The purpose of this Standard Operating Procedure (SOP) is to define the process for required the NIH StrokeNet Central Institutional Review Board (CIRB) reporting by sites engaged in National Institutes of Health (NIH) StrokeNet affiliated research. Sponsors and sites engaged in StrokeNet research are required to report unanticipated problems (including adverse events), injuries to subjects, protocol deviations/violations, changes initiated without CIRB approval to eliminate apparent immediate hazards to subject/s, complaints, non-compliance and cessation of research activities (collectively "required reports") that are determined, discovered, or learned by them in connection with the conduct of a StrokeNet human research study. This could also include any reports external to the trial site, including, but not limited to, Data Safety Monitoring Board (DSMB) reports and MedWatch reports. This SOP provides a description of these types of required reports and defines the standards, time frames, and procedures for these reports.

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.

Data Coordinating Unit (DCU): Data coordinating unit located at the National Data Management Center.

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

Investigator: A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

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

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

Prime Protocol Principal Investigator (PI): The individual 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. If this person is the IND or IDE holder, s/he is also responsible for all applicable FDA and NIH regulatory requirements, which includes all Sponsor-Investigator responsibilities.

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

Sponsor: An individual, company, institution, or organization that assumes or delegates responsibility for the initiation, management, regulatory reporting and/or financing of a clinical trial. Within the NIH StrokeNet model NIH funded trials are considered Investigator Sponsored Trials and certain agreed upon sponsor responsibilities can be delegated via the sub award process.

2. SCOPE

The policies and procedures in this SOP apply to parties involved with StrokeNet research, including the National Coordinating Center (NCC), the CIRB, the National Data Management Center (NDMC) and all StrokeNet Regional Coordinating Centers (RCC) and their Performance Sites (PS) engaged in StrokeNet research. For purposes of this SOP, a site is any institution that is engaged in StrokeNet research. The CIRB follows the University of Cincinnati Human Research Protection Program Policy HRP-092 for reporting unanticipated problems involving risks to participants and others, adverse events, and other problems to the IRB (see Attachment A).

3. PROCEDURES

A. CIRB Review Overview

Under the StrokeNet Reliance Agreement terms, the CIRB is responsible for reviewing required reports that are received, which can include UPIRTSO, protocol noncompliance issues, subject injuries, subject complaints, as well as protocol violations and deviations. The full list of reports can be found in Attachment A to this SOP. When reviewing any of the required reports, the CIRB is responsible for making the determination as to whether the report 1) constitutes UPIRTSO or 2) rises to the level of serious or continuing noncompliance with applicable laws and regulations or the requirements and/or determinations of the CIRB.

Based on its review, the CIRB must take appropriate responsive action, which may include submitting a report to regulatory agencies and/or suspension or termination of CIRB approval of the research. Any required reporting to regulatory agencies or oversight authorities, including OHRP, will be coordinated based on a process of discussion and consensus with the reporting site and its institutional officials. These discussions will include working together to determine the responsible party for reporting, including reporting any UPIRTSO to OHRP. Per OHRP guidance, any required reporting to regulatory agencies or oversight authorities must take place within one (1) month from receipt of the UPIRTSO report. In the case of suspension or termination of CIRB approval, the CIRB will notify NCC leadership, NINDS staff and site officials, including the PI, and appropriate Institutional Officials, within one (1) business day.

After determining the course of action, the CIRB must then inform the appropriate site(s) of the findings, determinations, actions taken, and any modifications or remedial action required by the CIRB in response to such report(s). In certain cases, such as when an adverse event is determined to be a UPIRTSO, the CIRB may determine that information contained in a report could impact

either subject safety or the conduct of the trial at all sites. In this instance, the CIRB will inform all site PIs engaged in the trial.

B. Event Reporting in WebDCU™

The following information is intended to provide event reporting guidance for investigators participating in StrokeNet trials inclusive of adverse events, serious adverse events, and unanticipated or unexpected problems involving risks to participants or others. The guidelines outlined herein incorporate common data elements and are in compliance with both the FDA and Health and Human Services (HHS) defined Code of Federal Regulations (CFR) for the protection of human research participants, the procedures and requirements governing the use of Investigational New Drug (IND), and the monitoring of serious and unexpected adverse events codified under Title 21 CFR part 56 (Institutional Review Boards), part 312 (Investigational New Drug) and 45 CFR part 46 (Protection of Human Participants).

Complete "Unanticipated Event-PD Report" (UAE-PD) located in WebDCU™ under "Project Management" → "Unanticipated Event-PD Report" and contact NCC Project Manager or CIRB Liaison for assistance if uncertainly exists surrounding need for event reporting. Events requiring prompt reporting will be submitted to the CIRB electronic protocol system by the NCC Project Manager on behalf of the site and will provide the site with CIRB letter of acknowledgement following CIRB review. Other deviations/violations, unanticipated problems, and/or complaints will be reviewed by the Prime Protocol Principal Investigator (PI) or delegate and the study team regularly.

C. Prime Protocol Principal Investigator (PI) Responsibilities for the Annual Continuing Review

The Prime Protocol PI will provide information listed below to the CIRB and attest to the following applicable requirements:

1. The Prime Protocol PI must submit a data report provided by the DCU to fulfill the requirement by the CIRB for the study team to evaluate the number of subjects enrolled in the research. This is to ascertain whether enrollment is consistent with the planned number of subjects described in the IRB-approved protocol.
2. The Prime Protocol PI must also submit a list of premature terminations (site withdrawals) provided by the DCU to fulfill the requirement of the CIRB for the study team to evaluate participant withdrawals for early identification of problems related to the conduct of the research.
3. The Prime Protocol PI must provide a summary of new and relevant information, published or unpublished, since the last IRB review that includes a synopsis from the Prime Protocol PI of the relevance of this information to the study's risks, benefits, alternatives and applicable informed consent documents.
4. The Prime Protocol PI must attest that the approved safety monitoring plan is being followed and that the DSMB has determined the research is appropriate to continue. The following requirements must be verified:
    a. The enrollment rate is reasonable to meet the goals of the study.
    b. Selection of subjects is equitable and meets the goals of the study.
    c. No events (deviation/violation, unanticipated problems, complaints, noncompliance, etc.) have occurred that alter the risk/benefit analysis and qualify as an unanticipated problem.
    d. No changes to the study are required to decrease deviations/violations, unanticipated problems, and/or complaints in the future.
5. The Prime Protocol PI must attest that the NDMC consent monitoring process is being followed to ensure that each site is using the appropriate consent and HIPAA form versions.

4. REFERENCES TO OTHER APPLICABLE SOPs and Guidance Documents

NINDS Guidelines for Data and Safety Monitoring in Clinical Trials, last updated August 8, 2013.
The NIH StrokeNet UAE-PD Reporting Guidelines, last updated May 3, 2021 (Attachment B).

5. LINKS:

http://researchhow2.uc.edu/home/browse-by-offices/hrpp

http://www.ninds.nih.gov/research/clinical_research/policies/data_safety_monitoring.htm

https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-

14_QuickReference_8.5x11.pdf)

6. DOCUMENT HISTORY

Version	Description of Modifications	Completion Date	Issue Date	Effective Date
1.0	Final	03-Jun-2014	03-Jun-2014	03-Jun-2014

2.0	September 2019 Revision	05-Sep-2019	22-Nov-2019	22-Nov-2019
2.1	Attached updated UC SOP	06-Feb-2020	06-Feb-2020	06-Feb-2020
3.0	Added Prime Protocol PI responsibilities for Continuing Review and administrative changes	29-Feb-21	29-Jun-21	29-Jun-21
3.1	Attached updated UC SOP	30-Jun-21	30-Jun-21	30-Jun-21

University of CINCINNATI

SOP: Reporting Unanticipated Problems Involving Risks to Participants and Others, Adverse Events and Other Problems to the IRB			
NUMBER	DATE	APPROVED BY	PAGE
HRP-092	4/5/2021	J. Strasser	1 of 6

1 PURPOSE

1.1 To ensure prompt reporting to the Institutional Review Board (IRB).

2 REVISIONS FROM PREVIOUS VERSION

2.1 Revised to remove duplications;

3 POLICY

3.1 Federal regulations require institutions to have written policies and procedures in place that ensure prompt reporting of unanticipated problems involving risk to participants or others and certain adverse events to the IRB, regulatory agencies and institutional officials. The University of Cincinnati IRB complies with all applicable local, state, and federal regulations that pertain to reporting requirements.

3.2 Unanticipated problems can occur in any type of research (medical or non-medical) and may include occurrences such as adverse events, research participant complaints, protocol deviations, and other untoward events involving risks to research participants or others. Events requiring prompt reporting by Investigators and research staff may involve physical, psychological, social, legal, or economic harms.

3.3 When research is not covered by DHHS regulations, reports of unanticipated problems involving risks to participants or others do not require OHRP reporting.

3.4 When research is not being conducted under IND or IDE applications, reports of unanticipated problems involving risks to participants or others do not require FDA reporting.

3.5 When following Department of Veterans Affairs (VA) regulations, guidance and policy for human subject research conducted at VA facilities:

3.5.1 For VA research, the terms "unanticipated" and "unexpected" refer to an event or problem that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population. The term "Unanticipated Problem Involving Risks to Subjects or Others" includes any event or problem that is serious, unexpected, and related to the research, where "related" means the event or problem might reasonably be regarded as caused by, or probably caused by, the research. Examples of serious unanticipated problems involving risks to participants or others may include:

- Interruptions of participant enrollments or other research activities due to concerns about the safety, rights, or welfare of human research participants, research staff, or others.
- Any work-related injury to personnel involved in human research, or any research-related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individuals, or leads to serious complications or death;
- Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the VA facility's research projects;
- Any Sponsor analysis describing a safety problem for which action at the VA facility might be warranted;
- Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research participants, research staff, or others;
- Any problem reflecting a deficiency that substantively compromises the effectiveness of the VA facility's HRPP.
- Deviations from the study protocol and/or research procedures that are likely to substantially affect 1) the rights, safety or welfare of the research

participant; 2) the participant's willingness to continue participation in the study; or 3) the integrity of the research data, including VA information security requirements.

Any serious adverse device effect on health or safety or any life-threatening problem or death caused by, or associated with a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including supplemental plan or application) or any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of research participants.

3.5.2 For VA personnel, local research deaths that are both unanticipated and related or possibly related to the research in a VA non-exempt research study must be immediately reported orally to the IRB of record and the ACOS/R&D within one business day. Written notification must follow within one business day of the study team becoming aware of the death. The IRB Chair or another qualified IRB voting member must assess and document whether any immediate actions are warranted to eliminate apparent immediate hazards to subjects within one business day and if so ensure those actions are initiated. Incidents may require the IRB to convene an emergency session prior to the next convened meeting. The IRB will review the initial written notification and the IRB Chair's (or qualified voting member's) immediate documented hazard assessment and any initiated actions at the next convened meeting, not to exceed 30 calendar days after the date of written notification. The IRB will determine and document within 30 calendar days of convened initial review whether 1) death was unexpected and related or possibly related to participation in the research, and 2) what, if any protocol or informed consent modifications are warranted. If modifications are warranted, the convened IRB must determine and document whether or not investigators must notify or solicit renewed/revised consent from previously enrolled research participants; and if so, when such notification or consent must take place and how it must be documented. The IRB must notify the CVAMC Director, RCO, and ACOS/R in writing of its determinations within 5 business days. If the IRB is unable to make a determination within 30 calendar days of the convened IRB's initial review due to insufficient information or due to the lack of sufficient time, then the IRB must notify the Director, RCO & ACOS/R in writing no later than 5 business days after the determination was due.

The unfounded classification of a serious adverse event as "anticipated" constitutes serious non-compliance.

3.5.2.1 VA personnel must submit written notification to the IRB within 5 business days after becoming aware of an apparent unanticipated problem involving risks to participants or others involving a VA non-exempt human participant research study. Within 5 business days after receiving a report of a serious unanticipated problem involving risks to participants or others, the convened IRB or a qualified IRB voting member must assess and document whether any immediate actions are warranted to eliminate apparent immediate hazards to research participants and, if so, ensure those actions are initiated. Incidents may require the IRB to convene an emergency session prior to the next convened meeting. The IRB will review the initial written notification and the IRB Chair's (or qualified voting member's) immediate documented hazard assessment and any initiated actions at the next convened meeting, not to exceed 30 calendar days

after the date of written notification. The IRB will determine and document within 30 calendar days of convened initial review whether 1) death was unexpected and related or possibly related to participation in the research, and 2) what, if any protocol or informed consent modifications are warranted. If modifications are warranted, the convened IRB must determine and document whether or not investigators must notify or solicit renewed/revised consent from previously enrolled research participants; and if so, when such notification or consent must take place and how it must be documented. The IRB must notify the CVAMC Director, RCO, and ACOS/R in writing of its determinations within 5 business days. If the IRB is unable to make a determination within 30 calendar days of the convened IRB's initial review due to insufficient information or due to the lack of sufficient time, then the IRB must notify the Director, RCO & ACOS/R in writing no later than 5 business days after the determination was due.

3.5.2.2 VA personnel must report serious or continuing noncompliance with applicable laws, regulations, policies, and agreements pertaining to non-exempt human research to the IRB within 5 business days after becoming aware. This includes, but is not limited to, serious or continuing noncompliance with the Common Rule, local VA medical facility policies and SOPs related to human research, if developed, IRB approved protocols, and the requirements or determinations of the IRB. Incidents indicative of a substantial safety risk may require that the IRB convene an emergency session prior to the next convened meeting. IRB reviews at the convened meeting will not exceed 30 calendar days after the date of written notification. The IRB will determine and document within 60 calendar days of the convened initial review 1) whether or not the event actually occurred and if so 2) what if any actions are needed to remediate problems or prevent future problems. If the IRB determines that serious or continuing noncompliance occurred, it must notify the Director, the RCO, and ACOS/R&D in writing of its determination and action within 5 business days after making the determinations.

3.5.2.3 The IRB will notify the VA medical facility director, the RCO and ACOS/R&D in writing within 5 business days of becoming aware of any of the following: 1) the suspension or early termination of a non-exempt VA human research study by the IRB or IO due to the study not being conducted in accordance with applicable regulations, policies, agreements, or IRB requirements or due to concerns about the safety, rights or welfare of human participants or others, if such suspension or termination is not otherwise reportable per the requirements noted above for reporting deaths, unanticipated problems involving risk to research participants or others or noncompliance. This written notification must include a statement of the reason for the action. 2) any change in the status (e.g., expiration, restriction, suspension, or termination) of the facility's FWA. 3) The termination or non-renewal of the HHS-OHRP registration of any IRB relied upon by the VA medical facility and oversight of VA research. 4) Failure of a VA medical facility to achieve or maintain full accreditation of its HRPP if such accreditation is sought.

3.5.2.4

3.6 Potential risks and adverse events that may be reasonably anticipated (i.e., "expected") must be described in the informed consent process/form and do not require prompt reporting to the IRB. The following are examples of events that DO NOT require prompt reporting:

- Adverse events or injuries that are BOTH not serious and unrelated;
- Adverse device effects that are non-serious, anticipated, or unrelated;
- Deaths not attributed to the research, e.g., from "natural causes," accidents, or underlying disease and the Investigator has ruled out any connection between the study procedures and the participant's death;
- Protocol deviations or violations not involving risks to participants or unlikely to recur;
- Data Safety Monitoring Board reports, interim analyses, or other reports, findings, or new information not altering the risk/benefit profile;
- Investigator Brochure updates not involving safety information; and
- Problems or findings not involving risk (unless the information could affect participants' willingness to continue in the research).

3.7 Adverse events (i.e., any untoward physical or psychological occurrence in a research participant including unfavorable and unintended events associated with the research procedures or investigational product) that do not meet the prompt reporting requirements described, and do not require reporting during the time of continuing review or otherwise unless the research team has determined that the frequency and severity of the events collectively would meet the criteria for prompt reporting.

3.8 The following events are potential examples of unanticipated problems involving risks to participants and others and shall be promptly reported:

- Internal adverse events that are unexpected, related to the research, and involve new or increased risks to participants or others ;
- Unanticipated adverse device effects
- Significant protocol deviations (or other accidental or unintentional changes to the protocol or procedures) involving safety or integrity risks or with the potential to reoccur;
- Events requiring prompt reporting according to the protocol Sponsor;
- Complaints made by research participants indicating an unanticipated event, or complaints that cannot be resolved by the research staff.
- Unapproved changes made to the research to eliminate an apparent immediate hazard to a research participant;
- Data and Safety Monitoring Board (DSMB) reports, interim analyses, or other oversight committee/monitoring reports/recommendations altering the risks/benefit profile;
- New information indicating an unexpected change in risks or potential benefits (e.g., literature/scientific reports or other published findings);
- Investigator's Brochure (IB or IDB) updates or revisions to safety information; and
- Other problems or findings (e.g., breach of confidentiality, loss of study data or forms, etc.) that could influence the safe conduct of the research.

3.9 External Adverse Events which are Unexpected, Serious AND suggest that the research places subjects or others at greater risk than was previously recognized and Related to the Research Intervention will be reported to the IRB within 30 working days of their receipt by the University/UC investigator. (Note: Only sponsor-generated safety reports that meet the Adverse Event reporting of the IRB should be submitted to the IRB.)

Ideally, adverse events occurring in subjects enrolled in a multicenter study should be submitted to a monitoring entity for review and analysis.

The report of the adverse event should include confirmation as to whether the external site reported the event to their IRB and to a monitoring entity.
The external adverse event reported to the IRB will be placed on a Committee agenda for review as determined by the IRB Chair or designee.
The University IRB may act with regard to the local study in response to the external adverse event (e.g., suspend the local study enrollment, but will not report the event to a federal agency or sponsor, unless required by the local action).

3.10 The IRB will accept reports when the Investigator is unsure whether the event should be reported, and the IRB will review such reports to determine whether the event meets the threshold requiring reporting.

3.11 All reports to the IRB of unanticipated problems will explain clearly why the event is "unanticipated" and clearly explain why the event represents a "problem involving risks to human subjects or others."

3.12 The UC IRB expects reports of unanticipated problems to include a corrective action plan to address the issue, or written justification for why none was provided.

3.13 Events identified as requiring prompt reporting will be reported to the IRB within 10 days of the research staff learning of the event.

3.14 Events resulting in temporary or permanent interruption of the study activities by the PI or Sponsor to avoid potential harm to participants must be reported immediately (within 48 hours).

3.15 Events that may represent unanticipated problems involving risks to participants or others shall be promptly reported, regardless of whether they occur during or after the study, or to a participant who has withdrawn from or completed study participation. If changes to the research or consent process are proposed as a result of the event, or if additional information will be provided to current and/or past participants, a modification request must be submitted for IRB review.

4 RESPONSIBILITIES

4.1 The principal investigator is responsible for ensuring promptly reportable events are identified and submitted to the IRB in a timely manner.

5 PROCEDURE

5.1 Research teams will report applicable occurrences that meet the criteria for prompt reporting with any applicable documentation to the IRB using "FORM: Reportable New Information (HRP-214)".

5.2 HRPP staff and/or the designated IRB member will review and assess the given occurrence and document conclusions, questions and/or concerns in the electronic record.

5.3 The IRB Chair or designee will inform the appropriate research team members, support units, administrative officials, funding/sponsoring organizations, and regulatory agencies of IRB determinations when needed and in accordance with applicable policies, procedures, agreements, and regulations.

6 MATERIALS

6.1 FORM: Reportable New Information (HRP-214)

6.2 HRP-024 – SOP – Review of Reportable New Information

7 REFERENCES

7.1 21 CFR §56.108(b)

7.2 45 CFR §46.103(b)(5), 45 CFR §46.108(a)

7.3 38 CFR 16 – VA regulations for human subject research protections, with informed consent and IRB regulations combined in one part.

7.4 VHA Directive 1200.05(1)(January 7, 2019, Amended March 3, 2020) — REQUIRMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

The NIH StrokeNet Unanticipated Event (UAE) and Protocol Deviation (PD) Report Guidelines for Site PIs (v5/3/2021)

Events Requiring Prompt Reporting

1. Certain events require prompt reporting by site principal investigators (PI). These are submitted via the WebDCU™ "StrokeNet UAE-PD Report".

Examples:

A. Internal adverse events that are unexpected, related to the research, and involve new or increased risks to participants or others (*2.7.1);

B. Unanticipated adverse device effects (*2.7.2);

C. Significant protocol deviations (or other accidental or unintentional changes to the protocol or procedures) involving safety or integrity risks or with the potential to reoccur (*2.7.3);

D. Events requiring prompt reporting according to the protocol Sponsor (*2.7.4);

E. Complaints made by research participants indicating an unanticipated event, or complaints that cannot be resolved by the research staff (*2.7.5);

F. Unapproved changes made to the research to eliminate an apparent immediate hazard to a research participant (*2.7.6);

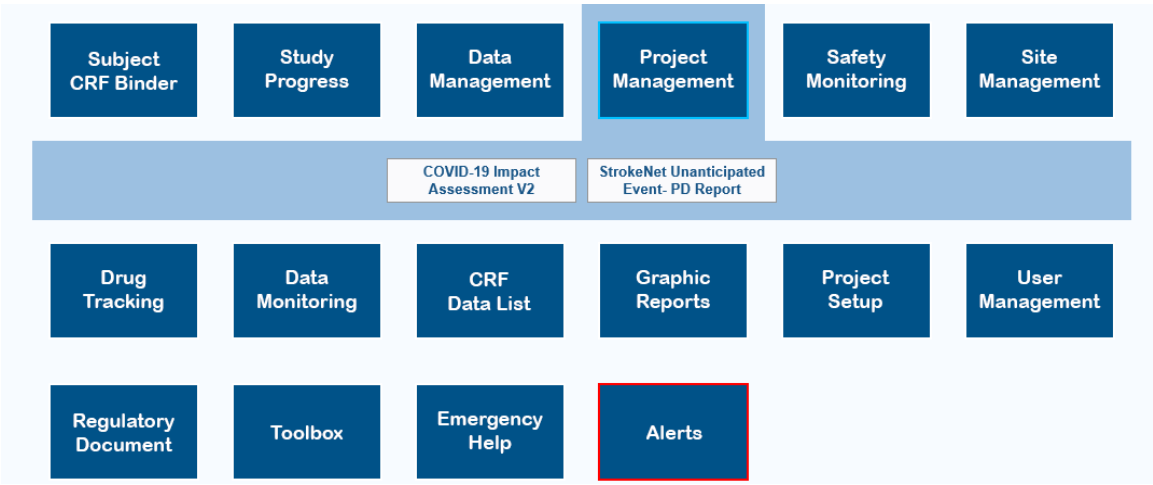
G. Problems or findings (e.g., breach of confidentiality, loss of study data or forms, etc.) that could influence the safe conduct of the research (*2.7.10).

H. Report any new information from written reports (i.e. study monitors, DSMB, etc.) (requirement from UAE-PD form)

** Based on Guidance for The NIH StrokeNet cIRB Event Reporting (HRP-092 SOP: Reporting Unanticipated Problems Involving Risks to Participants and Others, Adverse Events and Other Problems to the IRB)*

2. When an event occurs which requires prompt reporting, the Site PI will:

- Identify and assess the given incident, deviation, experience, or outcome.
- Document assessments and conclusions in the research record. Report any incident, deviation, experience, or outcome that meets the criteria **for prompt reporting** (see examples above) with appropriate documentation via the WebDCU™ "StrokeNet Unanticipated Event-PD Report" form. Contact NCC Project Manager for assistance if uncertainty exists surrounding need for event reporting.
- Inform the appropriate research team members, support units, administrative officials, funding/sponsoring organizations, and regulatory agencies about the event when needed and in accordance with applicable local policies, procedures, agreements, and regulations.



The NCC Project Manager will submit the event to the cIRB as Reportable New Information (RNI). The cIRB will provide a letter of acknowledgment that will be uploaded into WebDCU™ by the NCC Project Manager. If the cIRB requires further actions, the site will act on the letter requirements providing documentation of the completed requirements to the NCC Project Manager.

Reporting Other Events

Site PIs do NOT need to report specific trial events that do not rise to the level of an Unanticipated Problem Involving Risk to Subjects or Others (UPIRTSO) in the WebDCU™ "StrokeNet Unanticipated Event-PD Report" form **unless requested by NCC Project Manager**.

Examples:

A. Adverse events or injuries that are both: not serious and unrelated (*2.6.1);

B. Adverse device effects that are non-serious, anticipated, or unrelated (*2.6.2);

C. Deaths not attributed to the research, e.g., from "natural causes," accidents, or underlying disease and the Investigator has ruled out any connection between the study procedures and the participant's death (*2.6.3);

D. Protocol deviations or violations not involving risks to participants or unlikely to recur (*2.6.4);

Notes:

1. The Awardee Prime Protocol PI or delegate is responsible for monitoring these in an ongoing manner for events that individually, or in aggregate, should be reported to the cIRB as UPIRTSOs. The Awardee Prime PI will verify at the time of continuing review that:
   A. The approved safety monitoring plan is being followed.
   B. The DSMB has determined the research is appropriate to continue.
   C. No events (deviation/violation, unanticipated problems, complaints, noncompliance, etc.) have occurred that alter the risk/benefit analysis.
   D. No changes are required to decrease deviations/violations, unanticipated problems, and/or complaints in the future.

2. The DSMB, Sponsor, and StrokeNet Awardee Prime PI team also review events regularly per the trial safety monitoring plan.

References

1. The NIH ADM SOP 12: Central Institutional Review Board (cIRB) Reporting
2. HRP-092 SOP: Reporting Unanticipated Problems Involving Risks to Participants and Others, Adverse Events and Other Problems to the IRB