Data clarification requests (DCRs) may be initiated either by the SDMC, the Site Monitor, or the Site Manager. Notification of DCRs will be found on the WebDCU™ SHINE home page. DCRs must be responded to within 5 days.

13.4 Regulatory Documentation and E-Binder

All required regulatory documents, as found in the SHINE Regulatory Parameters Document (found on WebDCU™ under Project Management/Project Documents), must be uploaded into WebDCU™.

When a document is nearing expiration, the primary study coordinator will receive 30- and 7-day notices via e-mail. A weekly email will be sent if a site has any missing/rejected/expired regulatory documents outstanding.

13.5 Change in Study Personnel

13.5.1 Change in Site PI

Any changes in site PI must be approved by SHINE study leadership and the NIH.

13.5.2 Change in Other Study Personnel

Changes to site personnel during the study need to be updated in WebDCU™. The SHINE site manager or project director should be made aware of changes in the primary study coordinator to facilitate training. The following information is required to be uploaded into WebDCU™ for all additions/changes/deletions:

- All required regulatory documents
- Updated Delegation of Authority Log
- IRB approval for change in study team

13.5.3 Notifying SDMC about Changes in Study Personnel

The SDMC must be notified when study personnel are no longer affiliated with the trial. The Study Team Member table and User Permission Request tables located under the User Management tab must be updated, and the SDMC team will adjust WebDCU™ permissions.

14. Reports

14.1 Monthly Report

Reports can be generated from WebDCU™ to monitor trial progress and patient recruitment at each site. These reports will count the patients recruited overall and at each clinical site. They will also provide site-specific information on the number of subjects with missing or incomplete data in the WebDCU™ system (based on subject registration data), number of errors, follow-up visits completed and required procedures completed.

14.2 Enrollment Reports

Enrollment reports will be sent to NINDS annually summarizing data on subject accrual (overall and by site), date of first randomization and participant retention.

14.3 Newsletter

A newsletter may be sent to all site PI's and Study Coordinators. This newsletter will contain information on trial recruitment, updates and/or changes in the trial,

as well as any additional information, suggestions, reminders, or advice that may be appropriate or necessary.

14.4 DSMB Reports

A NIH-NINDS appointed independent DSMB will monitor all aspects of safety in this trial. Interim reports containing summary tables describing patient enrollment, baseline characteristics of patients, safety information, losses to follow up, outcome information, data quality information and any other information requested related to data integrity, continued relevance of the research questions, or patient safety will be provided every 6 months or as requested to the DSMB. The DSMB will follow the guidelines as described in the National Institutes of Health (NIH) issued policy on data and safety monitoring. The DSMB may pause or halt the trial at any time based on data from this or other trials. The DSMB will meet twice yearly unless otherwise determined. The results of all DSMB meetings will be summarized to the study PI and forwarded to site study teams for IRB submission at the enrolling institutions.

14.5 Recruitment and Retention Reports

The SHINE trial procedures include standards for monitoring sites for recruitment/enrollment performance. At the request of the trial's Data Safety Monitoring Board, the SHINE recruitment team reviews enrollments and reports findings to the SHINE Executive Committee regularly. On a quarterly basis, all NETT hubs and SHINE Ancillary sites are provided with a site-specific recruitment report.

15. Site Recruitment, Training and Initiation

15.1 Site Start-Up and Initiation

Prior to the enrollment of the first subject, site initiation will occur. Site initiation will take place by telephone (Readiness Call) after the site is deemed "Regulatory Ready". Sites will not be allowed to enroll subjects until all regulatory documents are complete. All regulatory documents must remain current throughout the course of the trial. It is the responsibility of the hub and/or ancillary site to ensure regulatory compliance is maintained at the enrolling site/spoke. The NETT-CCC will routinely monitor the WebDCU™ SHINE database for regulatory compliance.

Regulatory documents specific to the SHINE trial include:

- Investigator's Agreement Form
- Documentation of Full Study IRB Application Submittal
- IRB approval of SHINE Protocol/Full Study IRB approval
- IRB Approved Informed Consent Form
- Institutional Federalwide Assurance (FWA)
- Human Subjects Protection Policy
- Electronic Delegation of Authority Log (eDOA)
- CLIA
- Current Medical/Professional license
- Current CV
- NIHSS Certification
- mRS Certification