7. Data Collection and Management

7.1 SHINE CRF Collection Schedule

CRF #	CRFs	Screening	Baseline	Day 1 (0-24h)	Day 2 (24--48h)	Day 3 (48--72h)	**End of Treatment	Week 6 (+/- 14d)	Day 90 (+/- 14d)	End of Study
n/a	Screen Failure Log	X								
00	Eligibility Form		X							
07	Randomization		X							
01	Demographics		X							
02	Height and Weight		x							
03	Pre-Treatment Vital Signs		X							
04	NIH Stroke Scale		X						X	
05	HbA1c ****						X			
06	Adverse Event		OR	OR	OR	OR		OR	OR	
17	Hypoglycemic Event		OR	OR	OR	OR				
22	Neurological Worsening		OR	OR	OR	OR				
08	Lacunar Stroke Etiology						X			
09	Barthel Index								X	
10	Modified Rankin Scale							X	X	
11	SSQOL								X	
12	Unblinding Questionnaire- Study Participant								X	
13	Unblinding Questionnaire- Blinded Assessor								X	
14	End of Study									X
15	Study Treatment						X			
16	Antithrombotic Medications		X	X	X	X				
18	Medical History		X							
19	Glucose Control Medications		X				X		X	
20	Daily Care Log			X	X	X				
21	IV tPA and IA Therapy Form		*	*	*	*	X			
26	I-SPOT Eligibility Form		C							
24	Blood Sample Collection Form		C				C*****			
25	Blood Test Results		C				C*****			
23	QWSFS								C*****	

* Done daily. Form filled out at completion
** Completion of 72 hr treatment period unless discharged prior to 72 hrs
**** Indicates standard of care
C***** = Conditional for subjects participating in I-SPOT
O= Optional R= Repeatable X= Required C= Conditional for sites participating in I-Spot.

7.2 Overview

Data management will be handled by the NETT-SDMC which is housed in the Data Coordination Unit (DCU) at the Medical University of South Carolina (MUSC). All activities will be conducted in coordination with the NETT Network and the SHINE executive team. The data is managed using the WebDCU™ system which is a web-based database system developed by the MUSC DCU. It enables web-based real-time subject randomization, data entry and validation, project progress monitoring, subject tracking, user customizable report generation and secure data transfer.

7.3 Data Acquisition and Central Study Database

The entire study will be conducted using an electronic data acquisition method where all clinical data on enrolled subjects will be entered by the Spoke/Site personnel via the WebDCU™, a web-based Clinical Trial Management System. In order to provide user-friendly and easy-to-navigate interfaces, the WebDCU™ data capture screens are designed based on individual CRFs.

The latest version of each CRF is available as a PDF file on the study website. The most current version of the individual case report forms, as well as an up-to-date study book can be found on the study website. These may be used as worksheets and source documents.

The data validation procedure is implemented in two stages. The study database has extensive consistency checks programmed into the forms during the development of the database. These checks are in place to flag potential data entry errors and protocol violations, including missing required data, data out of a pre-specified range, data conflicts and disparities within each CRF and across different CRFs.

When data that violates the consistency check is entered, a rule violation message appears on the data entry screen alerting the data entry person to address it. The choices are:

(1) to correct the entry immediately;
(2) to correct the entry at a later time; or
(3) to dismiss the rule with an explanation if the entered data is confirmed to be correct. This may be done for warnings and protocol deviations. To do so, click the red rule violation to go to the 'View Record: Rule Violation' page. Click 'Data Confirmed' to dismiss the violation. Provide a reason before saving.

Secondly, for some checks that are more complicated, additional consistency checks are periodically run after data entry occurs at the site. All data items that fail these secondary consistency checks are queried via Data Clarification Requests (DCRs) within the database, by NETT-SDMC data managers. Site monitors are also able to generate Data Clarification Requests when discrepancies are found during source to database verification. The DCRs will be generated, communicated to the Spokes/Sites, and resolved on the secure study website. Any changes made in the system have a full audit trail.

7.4 Case Report Forms and Worksheets

7.4.1 Overview of Forms and Requirements

- Although it is not a requirement that you use paper worksheets for data collection, all data defined on the worksheets must be collected and entered into WebDCU™.
- If paper worksheets are used as source documents, they must be retained at the Clinical Site according to local and federal regulations.
- No data should be missing unless allowed by a skip pattern.
- If data for a numerical field is unknown or missing, please leave that field blank. Do not enter 0 (zero).
- Circles or radio buttons O indicate that you should choose only one answer.
- Boxes ☐ indicate that you should check all that
- Use the following format for all date fields: DD-MMM-YYYY (e.g., 31-JAN-2010)
- Complete dates should be entered, whenever possible, for all date fields. If the complete date isn't known, partial dates are allowed for select data points.
- In WebDCU™, use the following format for all time fields: 24 hour clock hh:mm

  Please note: 24:00 is not an allowable response. 24 hour clock time goes from 00:00 to 23:59. Midnight should be entered as 00:00.

Time on Clock	24 Hour Clock Time
12:00 AM	00:00
01:00 AM	01:00
02:00 AM	02:00
03:00 AM	03:00
04:00 AM	04:00
05:00 AM	05:00
06:00 AM	06:00
07:00 AM	07:00
08:00 AM	08:00
09:00 AM	09:00
10:00 AM	10:00
11:00 AM	11:00
12:00 PM	12:00
01:00 PM	13:00
02:00 PM	14:00
03:00 PM	15:00
04:00 PM	16:00
05:00 PM	17:00
06:00 PM	18:00
07:00 PM	19:00
08:00 PM	20:00
09:00 PM	21:00
10:00 PM	22:00
11:00 PM	23:00

- Name of person who collected the CRF data must be entered on the bottom of the paper worksheet, when the paper worksheet is used as a source document. This field will not be data entered but is required for monitoring purposes and should be dated and signed.

- Data Entry Timelines:
  - **Screen Failure Log - The Clinical Site staff should update the Screen Failure Log forms in WebDCU™ by the 10th of the following month.**
  - **Baseline through End of Study CRFs - Within 5 days of collection.**
  - **SAEs – Within 24 hours from the time the study team received knowledge of the event.**
  - ***Please note that site payments are dependent upon the subject's data being entered and submitted.***

- Data Clarification Request (DCR) Timelines: All responses to DCRs must be submitted within 5 days of query generation with the exception of DCRs for SAEs, which must be submitted within 24 hours of query generation.

7.5 Guidelines for Completion of Specific CRFs (See Appendix 8)

A comprehensive view of the SHINE CRF Completion Guidelines can be found in WebDCU by clicking on SHINE → project documents. A list of FAQs regarding the SHINE trial are also located in WebDCU → project documents under the tab 'Help Instructions'.

An example of an FAQ off 'Help Instructions'

Q: How do I remove a team member in SHINE?
A: Follow the instructions below:

1. Click on [User Management] tab, and then [User Permission Request].
2. On the list record page, click on the blue link in the # column to the left of the study team member name you are looking for.
3. Click on "Edit Record" located on the top right corner of the page. Remove all user group permissions by selecting the blank option in each drop down box on question 7. Once completed, click "Save Record." **Please be sure to add an end date for this user on the eDOA Log under section 5: Active Team Member.**
4. The data manager will then review and approve this request.

8. Adverse Events

8.1 Definitions

Adverse events will be defined and severity graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, found at http://evs.nci.nih.gov/ftp1/CTCAE/About.html.

8.1.1 Adverse Event

An adverse event (AE) is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. Non-serious adverse events will be reported from the time of randomization until the end of the study treatment period. The end of the study treatment period is defined as the infusion stop time, which may be prior to 72 hours from randomization. The only time that a non-serious AE is to be reported after the end of the study treatment period is a hypoglycemic event that occurs within 8 hours of stopping the study infusion and the study investigator determines to be possibly, probably or definitely related to the study treatment. See Section 8.2.2 for guidelines for assessing relatedness of hypoglycemic events that occur after the end of the study treatment period.

8.1.2 Serious Adverse Event

A serious adverse event (SAE) is any untoward medical occurrence that results in death, is life-threatening, requires or prolongs hospitalization, causes persistent or significant disability/incapacity, results in congenital anomalies/birth defects, or in the opinion of the investigators represents other significant hazards or potentially serious harm to research subjects or others.