CLINICAL STUDY DOCUMENT APPROVAL FORM

Study Name: Trevo Retriever Registry (China)

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Document Date or Version: **AC**

We, the undersigned, have read and approve the document specified above:

1. Name: **Donald Harkness** Functional Role: CPM Function Level: Director (D)

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5. Name: Functional Role: **Choose an item.** Function Level: Manager (M)

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Trevo® Retriever Registry (China)

Protocol

Version：AC

Study PI：Zhongrong Miao

Beijing Tiantan hospital, Capital Medical University

Sponsor：Stryker Neurovascular

Domestic agent: Stryker (Beijing) Medical Devices Co., Ltd.

Trevo® Retriever Registry (China)

Investigator's Signature Page

STUDY TITLE: **Trevo® Retriever Registry (China)**

STUDY CENTER: _____

(Print name of study center)

We, the undersigned, have read and understand the protocol specified above and agree on its content. We agree to perform and conduct the study as described in the protocol. In addition, when applicable, we agree to enlist sub-investigators who also agree to perform and conduct the study as described in the protocol.

Principal Investigator	Date
Print name:_____	DD/MMM/YYYY
Co- Principal Investigator (if applicable)	Date
Print name: _____	DD/MMM/YYYY

Trevo Retriever Registry Trial Investigator Agreement

I have read this Investigational Plan and agree to adhere to the requirements of this current version of the protocol.

I agree to personally conduct or supervise the research, and ensure all participating investigators and research staff are appropriately informed and trained prior to participating in any study related activities.

I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50, ICH E6 and institutional review board/Ethics Committee (EC) review and approval in 21 CFR Part 56 are met. I will ensure that the EC complies with the requirements of ICH E6 and 21 CFR Part 56 and will be responsible for the initial and continuing review and approval of the investigation. I agree to promptly report to the EC and to the Sponsor all changes in the research activity and all unanticipated problems involving risks to human subjects or others. I will not make any changes in research without EC approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in ICH E6, and/or the laws and regulatory requirements of the country in which the site is located.

I agree to maintain adequate and accurate records and to make those records available for inspection in accordance with ICH E6.

I agree to comply with all state and federal laws and regulations governing financial disclosure and to supply updated disclosure information, as it becomes known to me, during the course of the Trial and for one year following completion of the Trial, unless otherwise required by law or regulation.

I have not been restricted from participating in clinical research, nor is any action pending that could result in such restriction. If this occurs I shall provide immediate notification to the Sponsor.

I have NOT been involved in an investigation or other research that was terminated:

True□ False□ If False, please provide an explanation (including the circumstances that led to the termination):_____

Investigator Name (print)	Signature	DD/MMM/YYYY
Co-Investigator Name (print) □ N/A	Signature	DD/MMM/YYYY

Trevo® Retriever Registry (China)

Sponsor:	Stryker Neurovascular 47900 Bayside Parkway Fremont, CA 94538
Study Responsibility:	Dong Yu Manager, International Programs (China) Stryker Neurovascular 47900 Bayside Parkway Fremont, CA 94538
Study PI:	Zhongrong Miao, MD, PhD, Executive Director of Chinese Stroke Association (CSA) Chairman of China interventional neuroradiology society (CINS) Professor of Neurology and Neuroradiology Director of Interventional Neuroradiology Beijing Tiantan hospital, Capital Medical University
Study Centers:	Up to 15 Centers
Date of Issue:	November 27, 2017
Date(s) of Amendment(s):	NA

This protocol contains confidential information for use by the Investigators and their designated representatives participating in this clinical investigation. It should be held confidential and maintained in a secure location.

Trevo® Retriever Registry (China)

Protocol Synopsis

Study Objective	
Primary Objective	To assess real world performance of the Trevo® Retriever which is intended to restore blood flow in the neurovasculature by removing thrombus in subjects experiencing ischemic stroke
Primary Endpoint	Revascularization status assessment at the end of the procedure using the modified TICI score
Secondary Endpoints	1. Day 90 mRS assessment 2. Day 90 all-cause mortality 3. Neurological deterioration at 24 hours post procedure, defined as a four or more point increase in the NIHSS score from the baseline score 4. Rates of device and procedure related serious adverse events (AEs)
Other Key Assessments (Data points)	1. Time points will be collected on and not limited to the following: stroke symptom onset, admission to hospital/emergency department, start of Intravenous tissue Plasminogen Activator (IV tPA), angio suite arrival, arterial puncture, clot integration, Trevo removal and end of procedure (defined as the time of the final cerebral angiogram) 2. Data on the use of accessory products in conjunction with Trevo 3. Costs of hospitalization, discharge disposition 4. Analysis of imaging (pre, angio, post) by an independent core lab 5. Compare Day 90 outcome with pre-stroke mRS, baseline imaging and symptom onset to time of treatment.
Registry Device	Any approved Trevo Retriever approved for use by the local regulatory agency
Control	N/A
Device Sizes	All Trevo product sizes approved for use by the local regulatory agency
Study Design	
Study Design	Prospective, open-label, multi-center, China local registry
Planned Number of Subjects	200 subjects
Planned Number of Sites / Countries	Up to 15 sites
Primary Efficacy Parameter	Post-procedural Modified TICI score
Follow-Up Schedule	a. Day 30 telephone contact b. Day 90 clinic visit
Key Inclusion Criteria	1. Age ⩾18 2. Subjects experiencing acute ischemic stroke due to a large vessel occlusion who are eligible and suitable for restoration of blood flow using any approved Trevo Retriever in the neurovasculature to remove thrombus 3. Trevo Retriever is planned to be the primary mechanical neuro-thrombectomy device to remove the thrombus

	4. Subject or subject's legally authorized Representative (LAR) has signed the study Informed Consent Form 5. Subject willing to comply with the protocol follow-up requirements
Key Exclusion Criteria	1. mRS >2 2. Any known coagulopathy 3. Anticipated life expectancy less than 3 months 4. Known absolute contraindications to the use of required study medications or agents (e.g., heparin, aspirin, clopidogrel, radiographic contrast agents, etc.) 5. Preexisting neurological or psychiatric disease that would prevent complete the study required evaluations 6. The subject is participating in another mechanical neuro-thrombectomy device trial or any other clinical trial where the study procedure or treatment might confound the study end point.
Statistical Methods	
Statistical Test Method	There will be no sample size/or power estimation for this single-arm registry. Data analysis will be performed under guidance from the Study PIs, Steering Committee, and Sponsor.

Trevo® Retriever Registry (China)

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1 Introduction and Rationale

Stroke is the fifth most common cause of death and the leading cause of adult disability in the United States. Each year stroke afflicts approximately 795,000 Americans causing over 130,000 deaths. Stroke costs the nation $34 billion annually which includes the cost of medical care, medications and loss of productivity.[1] Around the world approximately 15 million people each year will endure a stroke resulting in an estimated 5.5 million deaths. Of those patients who are alive at 90 days after their stroke, 50% have some type of disability with 26% dependent on others for daily living and 20% require institutional care. One in six people worldwide will experience a stroke in their lifetime.[2-4] Good clinical outcomes in ischemic stroke have been shown to be strongly linked to revascularization.[5]

Intravenous tissue plasminogen activator (IV tPA) is the only FDA approved therapy for acute ischemic stroke and must be given within three (3) hours of ischemic stroke symptom onset. Unfortunately, only a small percentage of stroke patients receive IV tPA therapy, with estimates ranging from 2.4% to 9%. [6] Even so, the effect of IV tPA in patients in acute ischemic stroke has a short therapeutic time window [7-8] and is limited by the large thrombus burden that occurs in the setting of proximal arterial occlusion. One study reported that IV tPA has nearly no potential to recanalize occluded vessels with a thrombus length exceeding 8 mm. [9] When administered, IV tPA achieves early recanalization in only 30%–50% of subjects, with even lower recanalization rates in proximal large vessel occlusions (middle cerebral, basilar artery, and carotid terminus). Subjects who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment with the Trevo Retriever. The Trevo Retriever received CE mark on December 18, 2009 and was cleared by the FDA on August 13, 2012 to restore blood flow in the neurovasculature by removing thrombus in patients experiencing ischemic stroke within 8 hours of symptom onset. The Trevo Retriever also received FDA clearance on September 2, 2016 to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA). Patients should start treatment with the device within 6 hours of symptom onset.

2 Clinical Development Program for Trevo Retriever

The principal goal in treating acute ischemic stroke is to restore cerebral blood flow as rapidly and safely as possible. Two clinical trials, the Thrombectomy Revascularization of large Vessel Occlusions (TREVO) in acute ischemic stroke and the TREVO 2 study, were conducted using the Trevo Retriever. Both clinical studies demonstrated that mechanical neurovascular thrombectomy can safely and effectively be performed up to eight (8) hours after onset of acute ischemic stroke symptoms. [10-11]

2.1 TREVO Study

The TREVO study was a post marketing prospective, multi-center, single arm study performed at seven sites in Europe designed to quantify the performance of the Trevo Retriever in providing revascularization and clinical benefit to subjects experiencing a large vessel occlusion within 8 hours of symptom onset. The devices used in the study were the Trevo 4 x 20 mm, Trevo Pro 4, and Trevo 3 x 10 mm.

Sixty (60) subjects were enrolled between February 2010 and August 2011. Revascularization and intracranial hemorrhage at 24 hours were independently assessed by a central core lab. A Clinical

Events Committee (CEC) independently reviewed all protocol-defined safety endpoints to determine relationship to the device and the procedure, and the causes of all deaths.

The primary endpoint in TREVO was defined as angiographic revascularization as measured by the independent core lab using the TICI scale. Success was defined as a final TICI score of 2a or better. Post procedure, successful revascularization was achieved in 91.7% of subjects. In the TREVO study, operators were not restricted from using intra-arterial (IA) lytic, but it was only used in 10% of cases.

The secondary endpoints in TREVO were 90-day good clinical outcomes (defined as mRS of 0-2), 90 day mortality, device-related serious adverse events (DRSAEs) and symptomatic intracranial hemorrhage (SICH) at 24 hours (see **Table 1**).

Coincidentally, the rate of DRSAEs and SICH endpoints were both 5% (3/60), however the rates are not cumulative. One of the three SICHs was a DRSAE, while the other two were procedure-related. As mentioned above, one of the DRSAEs resulted in SICH while the other two DRSAEs were associated with subarachnoid hemorrhage (SAH).

Table 1. TREVO Study Primary and Secondary Endpoints [10]

Primary Effectiveness Endpoint	TREVO (N=60 subjects)
Revascularization	**91.7% (55/60)**
Secondary Endpoints	
90-Day Good Outcome (mRS = 0-2)	**55.0% (33/60)**
90-Day Mortality	**20.0% (12/60)**
Device-Related SAEs (DRSAEs)	**5.0% (3/60)**
SICH at 24 Hours (SITS-MOST)	**5.0% (3/60)**
SICH (ECASS III definition)	**8.3% (5/60)**

The TREVO protocol pre-defined specific events that were captured to assess safety which included vessel dissection, vessel perforations, ICH (as identified by core lab) and all deaths. Information for each of these events was collected and then independently adjudicated by the CEC. The results of this review are presented in **Table 2**. Most of the SAEs were attributed to the 12 deaths that occurred in the study, but a minority of the SAEs were related to the procedure (8.3%, 5 cases) or Trevo Retriever (5%, 3 cases).

Table 2. TREVO Adjudicated Safety Events [10]

Event	TREVO (N=60 subjects)
Serious Adverse Events (SAEs)	**21.7% (13/60)**
Procedure-Related SAEs	**8.3% (5/60)**
Device-Related SAEs	**5.0% (3/60)**

2.2 TREVO 2 Study

The TREVO 2 study was an IDE trial designed to support a 510k application for FDA clearance in the U.S. The trial [8] enrolled 178 subjects between February 3, 2011 and December 1, 2011 at 26 sites in the United States and one site in Spain. The subjects were randomized 1:1 to Trevo (N=88) or Merci (N=90) and were stratified by age and baseline NIHSS to ensure balance in the two arms. The devices used in the study were the Trevo 4 x 20 mm in 10 subjects, and the Trevo Pro 4 in 78 subjects. The subjects treated with Merci® Retrievers were treated with commercially available product, at the discretion of the treating physician.

The results for the primary effectiveness and safety endpoints are shown in the **Table 3**, and the results of the secondary endpoints are shown in **Table 4**.

Table 3. Primary Endpoint Results per the TREVO 2 (ITT population) [11]

Endpoint	Trevo (N=88)	Merci (N=90)	Difference [95% CI][a]	p-value
Primary Effectiveness Endpoint:				
Post-Device Revascularization Success (TICI 2a+)*	86.4% (76/88)	60.0% (54/90)	26.4% [13.2%, 39.0%]	< 0.0001[b] < 0.0001[c]
Primary Safety Endpoint:				
Composite Events ***	14.8% (13/88)	23.3% (21/90)	-8.6% [-20.7%, 3.2%]	0.1826[d]
Vessel Perforation	1.1% (1/88)	10.0% (9/90)	-8.9% [-17.0%, -2.2%]	
Intramural Arterial Dissection	0.0% (0/88)	1.1% (1/90)	-1.1% [-6.1%, 3.1%]	
Symptomatic ICH	6.8% (6/88)	8.9% (8/90)	-2.1% [-10.7%, 6.4%]	
Embolization to Previously Uninvolved Territory	6.8% (6/88)	4.4% (4/90)	2.4% [-5.0%, 10.3%]	
Access Site Complication Requiring Surgical Repair or Blood Transfusion	2.3% (2/88)	1.1% (1/90)	1.2% [-4.0%, 6.9%]	
Mortality within 24 hours	2.3% (2/88)**	0.0% (0/90)	2.3% [-1.9%, 7.9%]	
In vivo Device Failure	0.0% (0/88)	0.0% (0/90)	0.0% [-4.1%, 4.2%]	

Endpoint	Trevo (N=88)	Merci (N=90)	Difference [95% CI][a]	p-value
Other PR-SAE	0.0% (0/88)	0.0% (0/90)	0.0% [-4.1%, 4.2%]	

* Administration of IA t-PA was counted as a failure for post-device revascularization.
** One death that occurred within 24 hours was related to the device, the other was attributed to the index stroke.
***Patients who experienced more than one safety event are counted only once in the composite safety endpoint.
a: By normal approximation; b: non-inferiority hypothesis using Blackwelder's method with non-inferiority margin of 10%; c: One-sided Wald test of superiority; d: Fisher's exact test.

Table 4. Secondary Endpoints in TREVO 2 (ITT population) [11]

Endpoint	Trevo (N=88)	Merci (N=90)	Difference [95% CI][a]	p-value
Time to Revascularization (mins)[b] Mean ± SD (N) Median (min, max)	47.8±44.2 (79) 34.0 (6.0, 209.0)	47.3±38.8 (81)40.0 (4.0, 207.0)	0.5 [11.4%][c]	< 0.0001[d] 0.5326[e]
90-Day Good Outcome (Modified Rankin Score 0-2)	40.0% (34/85)	21.8% (19/87)	18.2% [4.2%, 31.7%]	0.0130[f]
90-Day Mortality	33.0% (29/88)	23.6% (21/89)	9.4% [-4.2%, 22.7%]	0.1845[f]
Asymptomatic ICH at 24 hours	40.9% (36/88)	53.3% (48/90)	-12.4% [-27.1%, 2.5%]	0.1017[f]
Neurological Deterioration at 24 hours[g]	15.9% (14/88)	22.2% (20/90)	-6.3% [-18.4%, 5.5%]	0.3418[f]

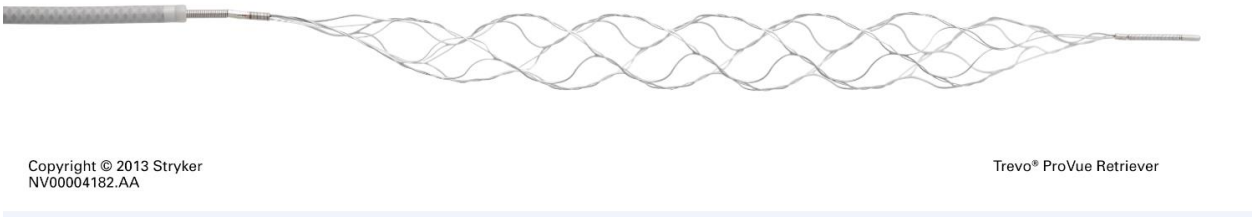
a: By normal approximation; b: Time to Revascularization was defined as the time from the start of the embolectomy procedure to achieving durable TICI 2a or better or to the end of the procedure if TICI 2a was not achieved. Subjects who had a baseline TICI score of 2a or did not have a study device used are excluded from this analysis (7 cases in Trevo arm, 8 cases in Merci arm); c: Per hypothesis testing setup, one-sided 95% upper confidence interval is used; d: One-sided Student's t-test of non-inferiority test with non-inferiority margin of 0.5 hours; e: One-sided Student's t-test of superiority test; f: Fisher's exact test; g: Defined as a four or more point increase in the NIHSS at 24 hours as compared to the baseline.

Overall the results of the TREVO and TREVO 2 trials demonstrate revascularization efficacy and safety of the Trevo Retriever.

3 Study Device Description

The Trevo Retriever is manufactured by Concentric Medical, a division of Stryker Neurovascular. The Trevo Retrievers consist of a self-expanding, laser cut, nitinol stent-like device permanently attached to a flexible, pusher wire. The retrievers have platinum markers at the distal end and platinum wires incorporated in the stent-like section to allow fluoroscopic visualization. (**Figure 1**). The packaged Retriever is pre-loaded into the Insertion Tool. The device has a hydrophilic coating to reduce friction during use and a shaft marker to indicate proximity of the Trevo tip relative to the microcatheter tip.

Figure 1: Trevo ProVue Retriever



During the procedure, the Trevo Retriever is delivered to the thrombus using a microcatheter. The microcatheter is then retracted to deploy the shaped section of the Retriever. The shaped section engages and traps the clot. The Retriever and microcatheter are pulled back to dislodge the thrombus. The Retriever, the thrombus, and the microcatheter are then removed from the body. Use of BGC (balloon guide catheter) and an intermediate catheter, such as DAC, are permitted but not required.

The Trevo Retriever has been designed and tested to perform multiple retrieval attempts in a single subject. Per the Instructions for Use (IFU), each Trevo Retriever may be used for up to three (3) retrieval attempts. After each deployment of the device it should be thoroughly cleaned and inspected before reloading. No more than six (6) retrieval attempts should be performed in the same vessel using any combination of retrieval devices. Refer to the IFU for detailed instructions on how to use the device. The Trevo Retriever should not be re-sterilized and reused.

There are no specific contraindications for the use of the Trevo Retriever apart from the inclusion and exclusion criteria of this Investigational Plan. Refer to the IFU for a listing of warnings and precautions.

Refer to the package (IFU) for further details and current information

3.1 Device Labeling

A copy of the device Instructions for Use (IFU) is included in each device package. The Trevo labels and labeling contain the following information:

- Lot Number
- Expiration date

4 Registry Objective

4.1 Primary Objective

To assess real world performance of the CFDA cleared Trevo Retriever intended to restore blood flow in the neurovasculature by removing thrombus in patients experiencing ischemic stroke.

4.2 Secondary Objective

To identify optimal interventional techniques, including type of anesthesia, access, and method of clot retrieval, to result in successful outcomes.

To provide robust registry data that maybe used to support expanded indications in regulatory submissions and support reimbursement dossiers.

To gather significant amount of real-world safety data to allow further subset analyses.

5 Registry Endpoints

Clinical data will be evaluated in all subjects where the Trevo Retriever is used as the primary thrombectomy device to remove thrombus from the neurovasculature in the setting of acute ischemic stroke.

5.1 Primary Endpoint

Revascularization status at the end of the procedure using the modified TICI score.

5.2 Secondary Endpoints

a. Day 90 mRS (good clinical outcomes defined as mRS of 0-2)
b. Day 90 mortality
c. Neurological deterioration at 24 hours, defined as a four or more point increase in the NIHSS score from the baseline score
d. Rates of device and procedure related serious AEs

5.3 Other Key Parameters of Interest

The following time points will be collected on the electronic Case Report Forms (eCRFs): stroke symptom onset, admission to hospital/emergency department, diagnostic imaging, start of IV tPA, angio suite arrival, arterial puncture, clot integration, Trevo removal and end of procedure (defined as the time of the final cerebral angiogram).

Other data points will be collected include, but not limited to: time for activation of stroke team and time for stroke team response, type of anesthesia (GA vs. CS) and patient presentation (airway at risk, combative).

Data on the use of accessory products during Trevo thrombectomy such as the balloon guide catheter (BGC), intermediate catheters and time to deliver all accessory products will be collected.

De-identified images will be sent to a core lab for adjudication (e.g. CT/MRI scans and angiographies).

Information will be collected on factors influencing health economics in the treatment of stroke. . The data collected will consist of hospital charges for cases involving real world use of the Trevo Retriever. Collection of health economic information shall be disclosed to the subject in the Informed Consent Form (ICF).

6 Justification for the Registry Design

The data results from the TREVO and TREVO 2 trials demonstrate revascularization efficacy and safety of the Trevo Retriever. The Trevo Retriever Registry is a prospective, open-label, multi-center, international trial. The purpose of the Trevo Registry is to assess the performance of the Trevo retriever in real world practice to increase knowledge on the performance of the device, monitor safety outcomes, detect rare complications, and to obtain information for potential improvements for next generation devices.

6.1 Method of Enrollment

Clinical data points will be evaluated in all subjects who meet the inclusion/exclusion criteria and where Trevo Retriever is used as the initial mechanical thrombectomy device to remove thrombus from the neurovasculature in the setting of acute ischemic stroke. For purposes of this registry, enrollment occurs when the Trevo Retriever is deployed through the compatible Microcatheter into the neurovasculature as the first mechanical neuro-thrombectomy device used to remove the thrombus.

A Screening and Enrollment Log will be maintained by each site to document basic information such as date screened and reason for screen failures for subjects who fail to meet the study eligibility criteria. In order to avoid bias, if a center chooses to participate in the Trevo Registry, every effort should be made to include all Trevo cases performed over a given duration of time in the registry. No site will be allowed to enroll more than 30% of the entire maximum study population unless first approved by Stryker.

7 Study Population

7.1 Selection Criteria

7.1.1 Inclusion Criteria:

1. Age ⩾18
2. Subjects experiencing acute ischemic stroke due to a large vessel occlusion who are eligible and suitable for restoration of blood flow using any approved Trevo Retriever in the neurovasculature to remove thrombus
3. Trevo Retriever is planned to be the primary mechanical neuro-thrombectomy device to remove the thrombus
4. Subject or subject's legally authorized Representative (LAR) has signed the study Informed Consent Form
5. Subject willing to comply with the protocol follow-up requirements

7.1.2 Exclusion Criteria:

1. mRS >2
2. Any known coagulopathy
3. Anticipated life expectancy less than 3 months
4. Known absolute contraindications to the use of required study medications or agents (e.g., heparin, aspirin, clopidogrel, radiographic contrast agents, etc.)
5. Preexisting neurological or psychiatric disease that would prevent complete the study required evaluations
6. The subject is participating in another mechanical neuro-thrombectomy device trial or any other clinical trial where the study procedure or treatment might confound the study end point.

7.2 Withdrawal and Replacement of Subjects

While study withdrawal is discouraged, subjects may withdraw from the study at any time, with or without reason and without prejudice to further treatment. Withdrawn subjects will not undergo any additional follow-up, nor will they be replaced. If a subject chooses to withdraw from the registry, the reason(s) for withdrawal will be recorded on the appropriate eCRF and in the medical record.

7.3 Enrollment Controls

Enrollment will be monitored to ensure no more than the specified number of subjects is enrolled. An electronic data capture (EDC) system will be used and the system will be monitored to ensure maximum enrollment is contained. All sites will be notified when enrollment is near the target. The electronic database will display a message announcing that target enrollment is reached.

8 Study Procedures

8.1 Written Informed Consent

A sample ICF is provided in **Appendix C** for the Investigator to prepare for use at the site. The written Informed Consent documents must be prepared in the language(s) of the potential subject population. The ICF must be approved by the Ethics Committee (EC) and a copy provided to Stryker Neurovascular. Modifications to the form must be approved by Stryker Neurovascular prior to implementation. The document version must be identified on the ICF to maintain version control.

Written Informed Consent must be obtained for all subjects prior to data entry into the Trevo Retriever Registry electronic database. The subject or the subject's legally authorized representative (LAR) will be asked to sign the ICF. Consent should be obtained pre-procedure but depending on subject's acuity the consent may be obtained up to seven days post-procedure. No data may be entered into the database until written consent has been obtained. In the absence of informed consent, an EC approved waiver of consent and executed data use agreement must be in place.

Study personnel should document the consent process in the subject's medical record per Good Clinical Practice (GCP). The subject or LAR is to be provided a copy of the signed ICF.

8.2 Pre-procedure Assessment

The following pre-procedure data will be collected:

- Confirmation that the subject meets the Inclusion/Exclusion criteria
- Demographics and medical history, including blood pressure and pre-stroke mRS
- Baseline Labs (PT, PTT, platelets, INR, glucose, pregnancy test if applicable)
- Baseline Medications
- Neurological examination including mRS and NIHSS assessments
- Determination of intracranial lesion location and if clot location is amenable for treatment utilizing the Trevo Retriever

8.3 Trevo Thrombectomy Procedure

Physicians should follow the most current IFU at all times with regards to the device compatibility, preparation and the recommended retrieval procedure. The Trevo thrombectomy procedure should be performed per the following general steps:

- Gain arterial access with 6F (or larger) Guide Catheter or BGC
- Place the appropriate Trevo Microcatheter distal to the clot
- Use of intermediate DAC for added support is optional
- Load the Trevo Retriever into the compatible Trevo Microcatheter using the insertion tool and advance to site of occlusion
- Pull back on the Trevo Microcatheter to unsheathe the Trevo Retriever within the clot

- After deploying the Retriever within the clot, visualize strut expansion and allow sufficient time for clot integration into the Retriever (approximately 5 minutes)
- If using a BGC, inflate the balloon to arrest flow
- Slowly pull the Trevo Retriever and Trevo Microcatheter back as a unit
- As the Trevo Retriever and microcatheter are being removed, begin vigorous aspiration through the guide catheter until the Trevo Retriever is removed from the subject

NOTE: Do not perform more than six (6) retrieval attempts in the same vessel. This total number applies for any combination of retrieval devices.

Immediately after each retrieval attempt with the Trevo Retriever, perform biplane angiography in order to assess the vessel patency in the neurovascular tree that is being treated. The same angiogram orientation should be used before and after the Trevo Thrombectomy procedure to assess the reperfusion status of the vessel(s).

- If reperfusion has been successful with the Trevo Retriever (recommended modified TICI score in the territory treated is ≥2b) the Trevo thrombectomy procedure should be stopped and no further interventions performed.
- If reperfusion has not been successful with the Trevo Retriever continue with additional retrieval attempts (up to the maximum allowed per the IFU). At any time during the procedure, adjunctive treatment (rescue therapy) may be initiated if deemed appropriate by the treating physician.

NOTE: The Trevo thrombectomy procedure should be terminated if any of the following occur:

- Neurological deterioration or alteration in function is detected leading to the suspicion of an intracranial hemorrhage.
- Evidence of intracranial hemorrhage on imaging is noted.
- The occlusion is refractory to six retrieval attempts in a single vessel.

Neurological deterioration or alteration in function leading to the suspicion of an intracranial hemorrhage will necessitate an emergent head CT or MRI scan. At the discretion of the treating physician, this evaluation may also include angiography or other diagnostic tests to determine the etiology of the clinical alteration. Management of an intracranial hemorrhage will be performed according to each institution's usual practice.

8.4 24 hours (-6/+24) post procedure

The following data will be collected at 24 hours (-6/+24) post procedure:

- NIHSS (see **appendix G**)
- SAEs related to the device or procedure.

- For all subjects who expire prior to the 24 hours (-6/+24) assessment, available information regarding the primary cause of death and date/time of death will be recorded, as well as, whether the subject was made "do not resuscitate" (DNR) or "comfort care only" prior to expiration.

Any death or SAE must be reported to Stryker Neurovascular within 24 hours of becoming aware of the event(s).

8.5 Discharge/Day 5-7 (whichever comes first)

A subject may be discharged from the hospital when clinically stable, at the Investigator's discretion. The following data will be collected at between Day 5-7 (if patient remains in the hospital) or at Discharge, whichever occurs first:

- NIHSS (see **appendix G**)
- mRS (see **appendix F**)
- SAEs related to the device or procedure
- Subject disposition at time of discharge
- For all subjects who expire prior to the Day 5-7/Discharge assessment, available information regarding the primary cause of death and date/time of death will be recorded, as well as, whether the subject was made DNR or "comfort care only" prior to expiration.

Any death or SAE must be reported to Stryker Neurovascular within 24 hours of becoming aware of the event(s).

8.6 Post Discharge Follow-up

The designated staff at the clinical site will review the study requirements with the subject to maximize compliance with the follow-up schedule. The staff will instruct subjects to return for follow-up assessments according to the study Time and Events Schedule in **Appendix D**. Study staff should establish a date for the follow-up visits with the subject and if possible, schedule the visits at the time of hospital discharge.

The study will be considered complete after all subjects have completed the Day 90 ± 14 follow-up assessments. Requirements of each follow-up evaluation are detailed below.

8.6.1 Day 30 (+ 14)

At Day 30 (+14 days) the following study assessments should be performed:

- mRS (see **Appendix F**) - A telephone assessment is conducted
- SAEs related to the device or procedure
- For all subjects who expire prior to the Day 30 assessment, available information regarding the primary cause of death and date/time of death will be recorded, as well as whether the subject was made DNR or "comfort care only" prior to expiration.

Any deaths or SAE must be reported to Stryker Neurovascular within 24 hours of becoming aware of the event(s).

8.6.2 Day 90 (± 14)

At Day 90 (± 14 days) the following study assessments should be performed:

- mRS score (see **Appendix F**) - If subject is unable to return to the clinic for the Day 90 visit, a telephone mRS assessment is preferable to no assessment
- SAEs related to the device or procedure
- For all subjects who expire prior to the Day 90 assessment, available information regarding the primary cause of death and date/time of death will be recorded, as well as whether the subject was made DNR or "comfort care only" prior to expiration.

Any death or SAE must be reported to Stryker Neurovascular within 24 hours of becoming aware of the event(s). .

9 Statistical Methods

9.1 Sample Size Estimate and Justification

There will be no sample size/or power estimation for this single-arm registry.

Two hundred subjects will be enrolled at up to 15 centers in China. Since recent positive data released from MR CLEAN and other stent retriever randomized trials, there are more research questions to be answered such as how the time to treat will affect the patient outcome and how image screening may contribute to patient selection. Data analysis will be performed under guidance from the Study PIs, Steering Committee, and Sponsor.

9.2 Analysis Populations

The Intent-to-treat principle will be followed to define the analysis population. All of the subjects who signed the informed consent and in whom Trevo Retriever was deployed through the microcatheter are considered enrolled and will be included in the analyses.

Sub-group analyses for the Registry will be performed under guidance from the Study PIs, Steering Committee, and Sponsor.

9.3 Statistical Analysis

All statistical analyses will be performed using SAS version 9.4 or above. (Copyright © 2002-2008 by SAS Institute Inc., Cary, North Carolina, USA, All rights reserved)

10 Data Management

10.1 Data Collection and Processing

Data will be collected in a secure, password protected electronic data capture (EDC) system, which is accessible via the Internet. All pertinent data will be entered by trained study center personnel into the electronic Case Report Forms (eCRFs). A unique subject ID number will be assigned to each subject. Every reasonable effort should be made to complete data entry within one week of data collection. For adverse reporting requirements refer to section 14. Any data discrepancies may be queried during ongoing review of data by the sponsor or may be identified and queried during routine remote data review process. Remote data review may be performed to verify data accuracy and ensure queries are resolved. The Principal Investigator or Sub-investigator must ensure the accuracy and completeness of the recorded data and provide his/her electronic signature on the appropriate eCRF.

Images sent to a Core Lab may also be entered into a separate EDC system. The core lab will ensure no personally identifiable information is available to the sponsor. Ongoing data review will be performed to identify possible data discrepancies. Manual and/or automatic queries may be created in the EDC system and will be issued to Core Lab for appropriate resolution.

11 Monitoring

The Sponsor is responsible for monitoring all data collected at the site to verify that the rights and wellbeing of subjects are protected, that trial data are accurate (complete and verifiable to source data) and that the trial is conducted in compliance with the protocol, GCP and regulatory requirements.

Data will be monitored for completeness and logical consistency. De-identified procedure summary, anesthesia record, must have the Trevo Registry subject identification number recorded on any forms sent to Stryker Neurovascular. The de-identified procedure documents may be compared against the eCRFs to ensure consistency for each subject enrolled.

Stryker Neurovascular will conduct an assessment of each participating site to assure that the investigators understand the investigational plan, as well as, their obligations to conduct the registry in accordance with applicable Regulations, GCP's and the registry protocol. The monitor will also confirm that the investigator has an adequate subject population, facilities, personnel and time to conduct the registry properly. Periodic monitoring visits may be made to confirm that the site remains compliant with the protocol, applicable Regulations, GCP and that all agreed-upon activities are carried out by the investigator and other specified staff members.

It is important that the Investigator and relevant study site personnel are available during monitoring visits and that sufficient time is devoted to the process. In order to perform her or his role well, the monitor must be given access to primary subject medical records which support the registry eCRFs. This access must be disclosed to the subject via the informed consent.

The investigator agrees to complete all registry requirements within three months of written notice of study completion. Continuation of the registry beyond this time must be mutually agreed upon in writing by both the investigator and Stryker Neurovascular.

Stryker Neurovascular will conduct a registry closeout meeting with each Trevo Registry site after the final data query is generated and data requests are addressed. The purpose of the closeout meeting is to confirm that all registry-related activities are complete and site personnel are aware of the regulatory obligations following study closure activities. The closeout meeting may transpire remotely e.g. teleconference or at an on-site monitoring visit. The closeout activities include but are not limited to the following:

- Final regulatory document review and collection of any outstanding documents including a copy of the investigator notification letter sent to the EC regarding completion of the Trevo Retriever Registry
- Address and close any open action items
- Discuss record retention requirements
- Review publication guidelines

12 Auditing

Sites may be subject to a quality assurance audit by Stryker Neurovascular or its designees, or other regulatory authorities who must be allowed access to eCRFs, source documents, and other study files.

It is important that the Investigator and relevant study personnel are available during any audits and that sufficient time is devoted to the process. The Sponsor audit reports will be kept confidential.

13 Device Accountability

There will be no device accountability or tracking as the Trevo Retriever has regulatory authorization to market the device.

14 Adverse Events

The following adverse events will be reported:

- all adverse events that occur during the procedure
- all SAEs related to the device or the procedure through Day 90
- all serious adverse events that result in death through Day 90

14.1 Adverse Event Definitions and Classification

Term	Definition	Reference
Adverse Event (AE)	Any untoward medical occurrence in a subject. This definition does not imply that there is a relationship between the adverse event and the device under investigation.	ISO 14155-1

Term	Definition	Reference
Adverse Device Effect (ADE)	Any untoward and unintended response to a medical device. *Note 1*: This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device. *Note 2*: This definition includes any event that is a result of a user error.	ISO 14155-1
Serious adverse event (SAE)	An adverse event that: • led to death • resulted in a life-threatening illness or injury • resulted in a permanent impairment of a body structure or a body function • required in-subject hospitalization or prolongation of existing hospitalization • resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function • led to fetal distress, fetal death or a congenital abnormality or birth defect	ISO 14155-1
Serious Adverse Device Effect (SADE)	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or if circumstances had been less fortunate.	ISO 14155-1
Unanticipated Adverse Device Effect (UADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report	ISO 14155-1

Underlying diseases are not reported as AEs unless there is an increase in severity or frequency during the course of the registry. Death should not be recorded as an AE, but should be reflected as an outcome to a specific AE.

14.2 Relationship

The Investigator must assess the relationship of the AE to the study device using the following criteria categories and definitions:

Unrelated - The AE is due to a concurrent illness or effect of another device/drug and is not related to the study device.

Related - The AE is due to the study device (possible, probable, or highly probable).

Unknown - The temporal relationship between the AE and study device cannot be clearly determined.

The Investigator must assess the relationship of the AE to the index procedure using the following categories and definitions:

Unrelated - The AE is due to a concurrent illness or effect of a drug and is not related to the index procedure.

Related - The AE is due to the index procedure (possible, probable, or highly probable).

Unknown - The temporal relationship between the AE and index procedure cannot be clearly determined.

14.3 Reporting Requirements

All required AEs (i.e. all AEs resulting in deaths and device and procedure related AE) will be recorded in the appropriate eCRFs.

All required SAEs and UADEs shall be reported within 24 hours of becoming aware to Stryker Neurovascular. The information can be emailed to the Stryker Neurovascular Safety Department personnel listed in Study Contacts List.

14.4 Device Failures, Malfunctions, and Product Nonconformities

All Trevo Retriever failures, malfunctions, and product nonconformities will be documented on the appropriate eCRF and the involved device(s) should be returned to Stryker Neurovascular for analysis if possible. Instructions for returning the study device(s) will be provided to the sites in their study binder. Device failures and malfunctions should also be documented in the subject's medical record.

All Trevo Retriever failures, malfunctions, and product nonconformities shall be reported within 24 hours of becoming aware to Stryker Neurovascular. The information can be emailed to the Stryker Neurovascular Safety Department personnel listed in the Study Contacts List.

NOTE: Trevo Retriever failures, malfunctions, and product nonconformities should be reported as soon as possible after becoming aware of them and are not to be reported as adverse events. However, if there is an adverse event that results from a device failure or malfunction, that specific event would be recorded on the appropriate eCRF. Trevo Retriever failures, malfunctions, product nonconformities and resulting AEs are reported to the Stryker Neurovascular complaint reporting system.

All Stryker Neurovascular non-study device malfunctions and nonconformities related to ancillary devices used in the procedure should be reported to the local Stryker Neurovascular customer service center. The customer service listing is provided in the study binder.

14.5 Reporting to Regulatory Authorities / IECs / Investigators

Stryker Neurovascular is responsible for reporting adverse event information to all participating investigators and regulatory authorities, as applicable.

The Site PI is responsible for informing Independent Ethics Committee (IEC) of UADEs and SAEs as required by local procedure. A copy of this report should be sent to Stryker Neurovascular.

15 Risk Benefit Analysis

The risks associated with this study are limited to a possibility that confidential patient information may be disclosed. It is possible that subjects enrolled into the Trevo Registry will receive no direct benefit from participation. Possible benefits of the registry include providing information regarding the use of the Trevo Retriever that may benefit future patients.

15.1 Risk Minimization

In order to minimize risks, Stryker Neurovascular will carefully select study sites and investigators who have experience with neuro-interventional procedures. Thorough training on the protocol, IFU and registry requirements will be conducted and Stryker Neurovascular will be available to address any registry specific issues or questions. Reasonable measures will be taken to minimize any risk of loss of confidentiality including the use of subject ID numbers for data entry and de-identification of any images or records sent to the core-lab or Stryker. A Steering Committee will assist in oversight of the Trevo Registry and Safety monitoring of the data will be continuous throughout the registry.

16 Steering Committee

The Trevo Retriever Registry will include a Steering Committee of up to 5 members or more of which one member may assume the Trevo Registry PI role. The Steering Committee will assist in oversight of the Trevo Registry with regard to protocol review and study progress. The Steering Committee will oversee dissemination of any study results through appropriate scientific sessions and publications. One of the Steering Committee members will Chair the publication committee. Interim analyses may be conducted and published throughout the study enrollment period based on the decision of the Steering Committee. The Steering Committee may select study investigators to participate on the publication committee. . The Steering/ Publication Committee will participate in the review and approval of all requests for data analyses, abstract and manuscript preparation and submission.

17 Ethical Considerations

17.1 Compliance with Good Clinical Practices (GCP)

The Investigator will ensure that this study is conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and that are consistent with GCP and applicable regulatory (local) requirements; whichever affords the greater protection to the subject.

17.2 Independent Ethics Committee

A copy of the protocol, proposed ICF, other written subject information, and any proposed advertising material must be submitted to the IEC for written approval. A copy of the written IEC approval of the protocol and ICF must be received by Stryker Neurovascular before recruitment of subjects into the Trevo Registry. The Investigator must submit and, where necessary, obtain approval from the IEC for all subsequent protocol amendments and changes to the ICF. The Investigator must notify the IEC of SAEs per IEC procedures, UADEs occurring at the site and other SAE/UADE reports received from Stryker Neurovascular in accordance with local procedures and regulations.

The Investigator is responsible for obtaining initial IEC approval and renewal throughout the duration of the registry. Copies of the Investigator's reports and the IEC continuance of approval must be sent to Stryker Neurovascular.

17.3 Protocol Adherence

Prior to beginning the study, the Investigator must sign the Investigator Agreement and Signature page documenting his/her agreement to conduct the study in accordance with the protocol. An Investigator must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. Each deviation from the protocol may be reported to the EC per local guidelines and government regulations. Protocol deviations are defined within **Appendix B**.

Stryker Neurovascular will ensure that this study is conducted in compliance with GCPs and all applicable regulatory requirements.

18 Study Administration

18.1 Pre-Study Documentation Requirements

Prior to enrolling any subjects into the registry the site must complete all pre-study essential documents, and these must be confirmed to be on file with the Stryker Neurovascular, including but not limited to: CV, signed clinical trial agreement; EC approval of the study and the Informed Consent; and all required study training. A site initiation visit will be conducted prior to authorization to enroll. No site may begin enrolling subjects until they receive written approval from the Stryker Neurovascular.

18.2 Record Retention

The Investigator will maintain all essential registry documents and source documentation, in original format, that support the data collected on the study subjects in compliance with the ICH/GCP guidelines. Documents must be retained for 2 years or longer per local governing Regulatory guidelines after a) the last approval of marketing application or b) formal discontinuation of the clinical investigation of the product. These documents will be retained for a longer period of time by agreement with Stryker Neurovascular or in compliance with other regulatory requirements. When these documents no longer need to be maintained, it is Stryker Neurovascular's responsibility to inform the Investigator. The Investigator will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If for any reason the Investigator withdraws responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility. Stryker Neurovascular must receive written notification of this custodial change.

18.3 Criteria for Terminating Study

Stryker Neurovascular reserves the right to terminate the study but intends only to exercise this right for valid scientific or administrative reasons and reasons related to protection of subjects. Investigators and associated EC will be notified in writing in the event of termination.

18.4 Criteria for Suspending/Terminating a Study Center

Stryker Neurovascular reserves the right to stop or suspend a study center at any time after the study initiation visit if no subjects have been enrolled, or if the center has multiple or severe protocol violations without justification or fails to follow remedial actions.

19 References

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12. English, J.D., Yavagal D.R., Gupta R., Janardhan V., Zaidat, O.O., Xavier, A.R., Nogueira, R.G., Kirmani, J.F., Jovin, T.G. Mechanical Thrombectomry-Ready Comprehensive Stroke Center Requirements and Endovascular Stroke Systems of Care: Recommendations from the Endovascular Stroke Standards Committee of the Society of Vascular and Interventional Neurology (SVIN). Intervent Neurol 2015:4:138-150.
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20 Appendices

Appendix A. Abbreviations

Abbreviation/ Acronym	Full Term
AE	Adverse Event
AHA	American Heart Association
Carotid T	Distal terminus of the carotid artery
CRA	Clinical Research Associate
CRF	Case Report Form
CSA	Clinical Study Agreement
CT	Computed Tomography
CTA	Computed Tomography Angiography
DRSAE	Device-related SAE
eCRF	electronic Case Report Form
GCP	Good Clinical Practices
IA	Intra-Arterial
ICH	Intracranial Hemorrhage
ID	Identification
IFU	Instructions For Use
IV	Intravenous
IV tPA	Intravenous tissue Plasminogen Activator
LAR	Legally Authorized Representative
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
PI	Principal Investigator
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect

SAH	Subarachnoid Hemorrhage
SBP	Systolic Blood Pressure
SICH	Symptomatic Intracranial Hemorrhage
TICI	(modified) Thrombolysis in Cerebral Infarction
t-PA	Tissue Plasminogen Activator
UADE	Unanticipated Adverse Device Effect

Appendix B. Definitions

Adverse Event (AE):	Any unintended disease or injury or untoward clinical sign in a research subject. NOTE - This definition does not imply that there is a relationship between the adverse event and the device under investigation.
Device Malfunction/Nonconformity:	The failure of a device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling for the device. The intended performance of a device refers to the intended use for which the device is labeled or marketed.
Embolization to New Territory:	Embolization into a previously uninvolved area of the brain, e.g. ACA embolization during MCA-M1 thrombectomy procedure.
Good Clinical Outcome:	A measure of neurologic functional outcome with a score of 0–2 on the modified Rankin Scale (mRS), usually assessed 90 days after treatment.
Irreversible Neurological Deterioration:	Neurological deterioration that is more than transitory, and is not related only to sedation. The neurological deterioration persists even after removal of sedation.
Modified Rankin Scale (mRS):	Scale for measuring the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability.
NIHSS Scale:	An assessment to objectively quantify the impairment caused by a stroke. It is composed of 11 items, each of which scores a specific ability between a 0 and 4. For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment. The individual scores from each item are summed in order to calculate a subject's total NIHSS score. The maximum possible score is 42, with the minimum score being a 0.
Pre-stroke disability:	Obtained at baseline, is representative of the subject's status before the index stroke, assessed by mRS on medical history obtained from subject, medical chart, or family members.
Protocol Deviation:	This protocol does not require specific interventions, therefore the term deviation will only be used to describe the following situation: Failure to obtain informed consent per Good Clinical Practices (GCP).
Serious Adverse Device Effect (SADE):	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or if circumstances had been less fortunate.

Serious Adverse Event (SAE):	An adverse event in a research subject that led to a death, or led to a serious deterioration in the health of the subject that resulted in a life-threatening illness or injury, or resulted in a permanent impairment of a body structure or a body function, or required in-subject hospitalization or prolongation of existing hospitalization, or resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function. SAEs are a subset of AEs.
Subarachnoid Hemorrhage (SAH):	Bleeding into the subarachnoid space - the area between the arachnoid membrane and the pia mater surrounding the brain.
Symptomatic ICH (SICH):	The primary protocol definition is adapted from ECASS III as any apparently extravascular blood in the brain or within the cranium that is associated with clinical deterioration as defined by an increase of four points or more in the NIHSS or that led to death and was judged to be the predominant cause of a neurologic deterioration. SITS-MOST definition is any PH-2, defined as dense hematoma > 30% total of the infarcted area with substantial space-occupying effect or any hemorrhage area outside the infracted area.
Unanticipated Adverse Device Effect (UADE):	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

Trevo® Retriever Registry (China)

Appendix C. Study Informed Consent Form Template

Trevo® Retriever Registry (China)

Appendix D. Time and Events Schedule

Time and Events Schedule						
Assessments:	**Pre-procedure (Screening /Baseline)**	**Procedure**	**24 (-6/+24) hrs post procedure**	**Discharge (or Day 5-7 whichever comes first)**	**Day 30 +14 days**	**Day 90*** ±14 days**
Inclusion/Exclusion Criteria	✔					
Informed Consent*	✔					
Demographics and Medical History	✔					
Baseline Medications	✔					
Baseline Labs (PT, PTT platelets, INR, glucose). Pregnancy test, if applicable	✔					
mRS**	✔			✔	✔	✔
NIHSS assessment	✔		✔	✔		
Stroke onset/etiology	✔			✔		
CT/MR[ﾝ]	✔		✔			
Angiogram Procedure Information [‡***ﾝ]		✔				
Hospital Stay/Discharge Disposition				✔		
Post Discharge Follow-up****					✔	✔
Adverse Events[‡]		✔	✔	✔	✔	✔
Utilization/Economic measures[‡‡]				✔		✔
Study Completion						✔

*Written IC must be obtained prior to any data entry.
**Telephone mRS assessment is acceptable if subject not able to return to the clinic in person.
****Study Staff should review the study requirements with the subject and arrange all follow-up visits at discharge.
[‡] All AE during procedure and only DR and PR SAE, death post procedure.
[‡‡]De-identify forms and enter subject ID # prior to sending to Stryker
ﾝ CT/MR and Angiographic images will be de-identified with subject ID# if submitted to SNV or the core lab.

Appendix E. Modified TICI Perfusion Categories

Grade 0: No Perfusion. No antegrade flow beyond the point of occlusion.

Grade 1: Penetration with Minimal Perfusion. The contrast material passes beyond the area of obstruction but fails to opacify the entire cerebral bed distal to the obstruction for the duration of the angiographic run.

Grade 2: Partial Perfusion. The contrast material passes beyond the obstruction and opacifies the arterial bed distal to the obstruction. However, the rate of entry of contrast into the vessel distal to the obstruction and/or its rate of clearance from the distal bed are perceptibly slower than its entry into and/or clearance from comparable areas not perfused by the previously occluded vessel, e.g. the opposite cerebral artery or the arterial bed proximal to the obstruction.

Grade 2a: Partial filling with <50% of the entire vascular territory is visualized.

Grade 2b: Partial filling with ≥50% of the entire vascular territory is visualized. If complete filling of all of the expected vascular territory is visualized, the filling is slower than normal.

Grade 3: Complete Perfusion. Antegrade flow into the bed distal to the obstruction occurs as promptly as into the obstruction and clearance of contrast material from the involved bed is as rapid as from an uninvolved other bed of the same vessel or the opposite cerebral artery.

Reference

Higashida RT, Furlan AJ, Roberts H, et al., *Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke.* Stroke, 2003. 34:e109–137

Appendix F. Modified Rankin Scale (mRS)

0 - No symptoms at all

1 - No significant disability despite symptoms; able to carry out all usual duties and activities

2 - Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance

3 - Moderate disability; requiring some help, but able to walk without assistance

4 - Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance

5 - Severe disability; bedridden, incontinent and requiring constant nursing care and attention

6 - Dead

Reference

Bonita R, Beaglehole R. *Modification of Rankin Scale: Recovery of motor function after stroke*. Stroke. 1988. 19 (12): p. 1497-1500

Appendix G. National Institute of Health Stroke Scale (NIHSS)

Reference

National Institute of Health, National Institute of Neurological Disorders and Stroke Scale. https://www.ninds.nih.gov/sites/default/files/NIH_Stroke_Scale.pdf