Trevo® Retriever Registry

Investigator's Signature Page

STUDY TITLE: **Trevo® Retriever Registry**

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 (IRB/EC) review and approval in 21 CFR Part 56 are met. I will ensure that the IRB/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 IRB/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 IRB/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

Sponsor:	Stryker Neurovascular 47900 Bayside Parkway Fremont, CA 94538
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Study Centers:	Up to 100 sites worldwide
Date of Issue:	16 JUL 2013 Protocol Number CDM10000023 Rev AA
Date(s) of Amendment(s):	26 MAR 2015 Protocol Number CDM10000023 Rev AB 24 MAR 2016 Protocol Number CDM10000023 Rev AC

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

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 the following: stroke symptom onset, admission to initial hospital/emergency department, if transferred, time of arrival to second hospital, diagnostic imaging, start of Intravenous tissue Plasminogen Activator (IV tPA), angio suite arrival, arterial puncture, time of each Trevo pass, 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. Health economics, costs of hospitalization, length of stay, discharge disposition 4. Sub-study analysis of imaging (pre, angio, post) with an independent core lab measurement of ASPECTS, collaterals, modified TICI scores and core infarct volume. 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, consecutive enrollment, multi-center, international registry
Planned Number of Subjects	Up to a maximum of 2000 subjects
Planned Number of Sites / Countries	Up to 100 sites worldwide
Efficacy Parameters	Post-procedural Modified TICI score
Follow-Up Schedule	a. Day 30 telephone contact b. Day 90 clinic visit
Key Inclusion Criteria	1. Subjects experiencing acute ischemic stroke who are eligible for restoration of blood flow using any approved Trevo Retriever in the neurovasculature to remove thrombus 2. Trevo Retriever is the initial mechanical neuro-thrombectomy device used to remove the thrombus

	3. Signed Informed Consent obtained 4. Subject willing to comply with the protocol follow-up requirements 5. Anticipated life expectancy of at least 3 months
Key Exclusion Criteria	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

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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.

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%]	
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 1a and 1b**). 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 Microcatheter tip.

Figure 1a: Trevo Retrievers

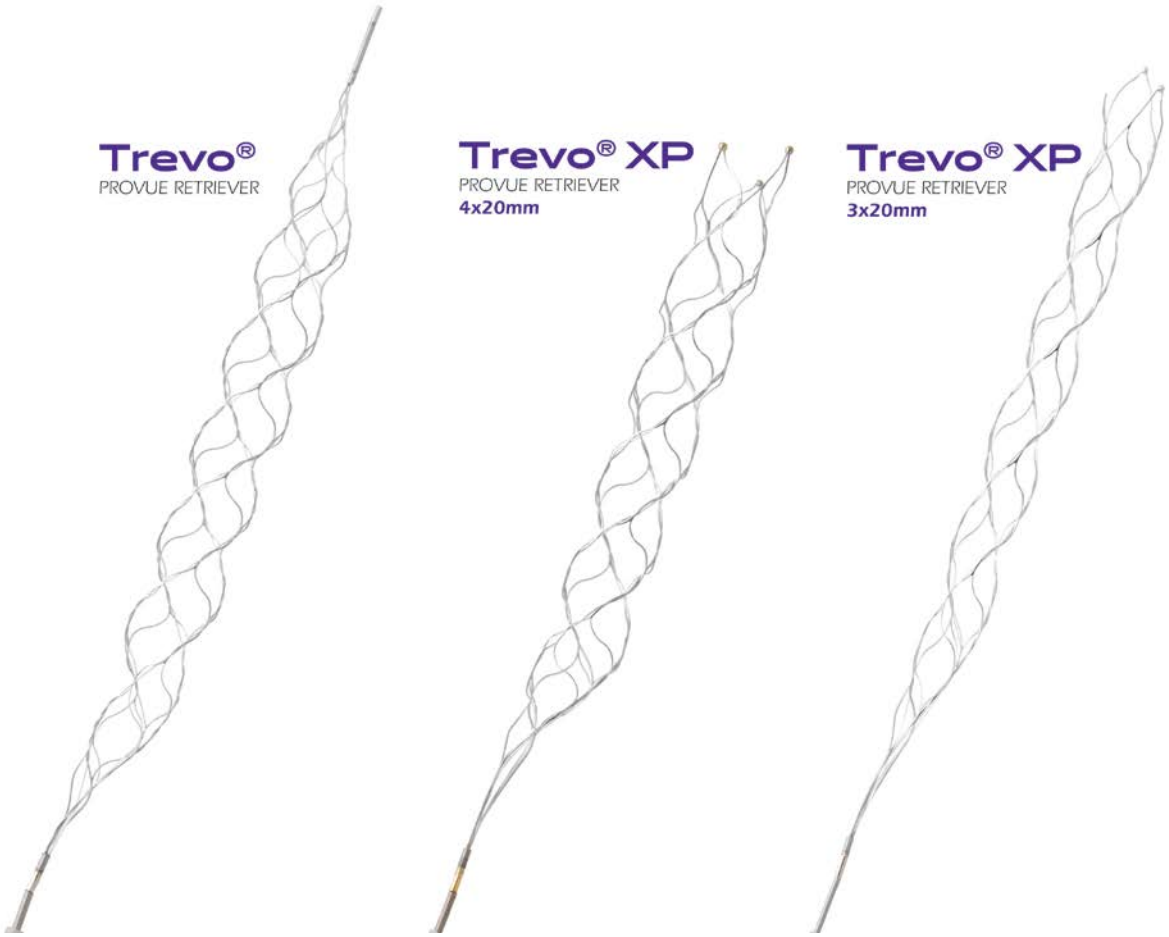

Figure 1b: Trevo Retrievers under fluoroscopy visualization

During the procedure, the Trevo ProVue 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.

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.

All Trevo Retriever models (e.g. Trevo® ProVue™, Trevo® XP ProVue™) and device sizes will be allowed in the Trevo Registry upon receipt of local regulatory agency approval.

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:

- Device Dimensions
- Lot Number
- Expiration (use before) date
- Microcatheter Compatibility

4 Registry Objective

4.1 Primary Objective

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

5 Registry Endpoints

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

5.1 Primary Data point

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

5.2 Secondary Data points

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 Assessments (Data points)

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

Data on the use of accessory products during Trevo thrombectomy such as the balloon guide catheter (BGC) and intermediate catheters such as the distal access catheter (DAC) will be collected.

De-identified images may 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 such as costs of hospitalization, length of hospital stay and discharge disposition. The data collected will consist of hospital charges for cases involving real world use of the Trevo Retriever. . The UB-04 form will be collected within the United States while in other countries a CRF containing similar information will be completed. 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, consecutive enrollment, 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 15% (300 subjects) of the entire maximum study population unless first approved by Stryker.

7 Study Population

7.1 Selection Criteria

7.1.1 Inclusion Criteria:

1. Subjects experiencing acute ischemic stroke who are eligible for restoration of blood flow using a Trevo Retriever in the neurovasculature to remove thrombus
2. Trevo Retriever is the initial mechanical neuro-thrombectomy device used to remove the thrombus
3. Signed Informed Consent obtained
4. Subject willing to comply with the protocol follow-up requirements
5. Anticipated life expectancy of at least 3 months

7.1.2 Exclusion Criteria:

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 that 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 (within 15 subjects to maximum enrollment). 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 study Institutional Review Board (IRB)/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 IRB/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 (recommended modified TICI score in the territory treated is ≥2b) 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.

If adjunctive treatment (rescue therapy) is used AFTER the Trevo Retriever, biplane angiography should be performed immediately afterwards in order to reassess vessel patency and determine the effect of the adjunctive rescue treatment. The last angiogram prior to the use of rescue therapy will be considered when rating post-Trevo Retriever reperfusion.

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 by eCRF completion.

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 by eCRF completion

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 by eCRF completion.

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
- De-identify copies of heath economic forms such as completed UB-04 Claims Forms, or equivalent claims forms per Country will be provided to Stryker with the registry subject number of the forms
- 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 by eCRF completion.

9 Statistical Methods

9.1 Sample Size Estimate and Justification

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

In order to conduct sub-group analyses and detect rare complications, of real world data a sample size of 2000 will provide more data for the further subgroup analysis. With total 2000 subjects, additional analysis of comparing TICI scores or 90 days mRS among the different locations could be carried out. Since recent positive data released from MR CLEAN and three 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.

Day 90 outcomes will be compared to pre-stroke mRS status, baseline imaging and time of symptom onset to treatment. The first interim analysis will be performed after 300 subjects are enrolled and the results will be reported. Additional interim analyses and data reporting will occur throughout the study enrollment period.

9.3 Statistical Analysis

All statistical analyses will be performed using SAS version 9.2 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. Any data discrepancies may be queried during ongoing review of data by the sponsor or may be identified and queried during routine remote monitoring process. Remote monitoring 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.

If images are sent to a Core Lab the results may also be entered into the EDC system and may be electronically signed by the reviewer responsible for entering this data. Ongoing data review will be performed to identify possible data discrepancies. Manual and/or automatic queries will be created in the EDC system and will be issued to Core Lab for appropriate resolution.

11 Monitoring

Data will be monitored remotely for completeness and logical consistency. De-identified procedure summary, anesthesia record, Trevo Registry worksheets and UB-04 forms or equivalent claims forms per country 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 enrollment 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 IRB/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.

It is important that the Investigator and relevant study personnel are available during any audits and that sufficient time is devoted to the process.

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 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
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

Term	Definition	Reference
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 via data entry into the eCRFs. If access to eCRFs is not available then the information can be faxed to the Stryker Neurovascular Safety Department personnel listed in current Study Contacts List provided in the study binder.

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 via data entry into the eCRFs. If access to eCRFs is not available then the information can be faxed to the Stryker Neurovascular Safety Department personnel listed in the current Study Contacts List provided in the study binder.

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 / IRBs / 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 the IRB/ 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. The Steering Committee will prepare a manuscript for publication of the interim analyses that will begin after 300 subjects have been enrolled. Subsequent interim analyses may be conducted and published throughout the study enrollment period. The Steering Committee may select study investigators to participate on the publication committee. These additional publication committee members are chosen based on enrollment, adherence to the protocol and protocol deviation rates. 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 Institutional Review Board/Independent Ethics Committee

A copy of the protocol, proposed ICF, other written subject information, and any proposed advertising material must be submitted to the IRB/IEC for written approval. A copy of the written IRB/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 IRB/IEC for all subsequent protocol amendments and changes to the ICF. The Investigator must notify the IRB/IEC of SAEs per IRB/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 IRB/IEC approval and renewal throughout the duration of the registry. Copies of the Investigator's reports and the IRB/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 must be documented with the date and reason for the deviation and reported to the Stryker Neurovascular as soon as possible, and to the IRB/EC per local guidelines and government regulations. Major and minor 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, medical license, W-9 or W-8, and signed clinical trial agreement; IRB/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 IRB/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.

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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.
Device-Related Serious Adverse Event (DRSAE):	Trevo device related vascular perforation or intramural arterial dissection, symptomatic ICH, embolization to a new territory, intra-procedural death, or device failure (*in vivo* breakage).
Distal Embolization (DE):	Any downstream occlusion distal to the target artery lesion, into the target ischemic territory, is considered DE unless complete angiogram or pre procedure non-invasive imaging demonstrated patency of these distal branches.
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.
Procedure-Related Serious Adverse Event (PRSAE):	Procedure-related events that include, but are not limited to vascular perforation or intramural arterial dissection, symptomatic ICH, embolization to a new territory, or access site complication requiring surgical repair or blood transfusion, intra-procedural death, or device failure (e.g. *in vivo* breakage).

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.

Appendix C. Study Informed Consent Form Template

You may be eligible to take part in a data collection study called the Trevo® Retriever Registry. This form will give you important information about why the research registry is being done, what will happen during the registry, and the risks and possible benefits. Please read it carefully. This consent form may contain words that are new to you. If you read any words that are not clear, please ask the person who gave you this form to explain them to you. You may also want to talk to family, friends, your primary care doctor, or other health care provider about joining this study. If you decide that you would like to take part in the study, you will be asked to sign and date this form and you will be given a copy of the signed form to keep.

Investigator/ Hospital	Insert name and Hospital
Sponsor	Stryker Neurovascular

Introduction and Purpose

The purpose of this Trevo Registry is to collect information (data) on a medical device called the Trevo Retriever. The registry will also collect data on other standard of care treatments and increase our understanding that the treatment has on stroke patients. You have been asked to participate in the registry being conducted by <Dr's name> at <site name> because you had a stroke.

The type of stroke that you had occurs when there is a blood clot that stops the flow of blood to an artery in your brain. This type of stroke can be treated in many ways, including the use of drugs to try to dissolve the blockage, the use of devices (like the Trevo Retriever) to remove the blood clot, and the use of therapeutic treatments that prevent stroke from happening or help you get better after having a stroke. This registry will collect data on the usage of the Trevo Retriever which is a type of stent (a small metal mesh tube) that is made to be put into your brain to grab the clot and pull it out to unblock the blood vessel. The Trevo Retriever does not stay in your body. The Trevo Retriever is not investigational or experimental and has received approval to sell and be used in the USA, Europe, and other countries.

You were chosen as a possible participant in the Trevo Retriever Registry because your doctor may use or may have used the Trevo Retriever to treat your stroke.

The Trevo Registry is expected to include about 2000 patients from approximately 100 hospitals around the world.

The Trevo Registry will collect data from your medical records starting from the time you are admitted to the hospital through your 90 day checkup visit with your doctor. Information about your health history, demographics, blood tests, brain imaging exams, treatment, and cost of your treatment and hospital stay will be collected. The brain image testing conducted during your hospitalization may be reviewed by a core lab that will provide an independent central assessment of the images. After you leave the hospital, the registry staff will ask you, or a family member, for a health check on your ability to do daily activities at 30 and 90 days after your treatment.

Whether or not you participate in this data collection registry, you will be given the same standard of care as all stroke patients at this hospital. Currently, standard care for stroke patients may include, but is not limited to the following:

- Physical exam and medical history
- Neurological and functional tests
- Routine blood tests
- Neurological imaging studies such as a CT (computed tomography) or MRI (magnetic resonance imaging)
- Treatment using a "clot busting" drug to break up the clot such as tissue plasminogen activator (t-PA)
- Cerebral angiogram
- Interventional radiology procedure(s) to treat a blocked artery using a device like the Trevo Retriever
- Other routine supportive therapies

You need to tell your doctor your medical history, especially if you are pregnant, have drug allergies, or have allergies to any metals or plastics, and if you are taking any medications. You and your doctor will determine which treatment choices are best for you.

Potential Benefits of Participating

The data collected on your treatment will be used to better understand how stroke diagnosis, treatment, and outcomes are related. Additionally the data will further direct the development of future stroke research studies. Your participation may help decide the best treatment to reduce health care costs related to stroke care while improving outcomes. We cannot and do not guarantee or promise you will receive any benefit from the registry.

Potential Risks by Your Participation

There are no risks involved with data collection in this registry. However, there may be a risk of loss of confidentiality. All efforts will be made to ensure that your health information remains confidential. The research staff will take every measure possible to protect your confidentiality. Please refer to the section titled "Confidentiality" and the "HIPAA Authorization Form" attached to this consent for more information about your personal health information. There are no other known risks to you for allowing the study doctor to collect information about you and the treatment you receive for your acute ischemic stroke.

Trevo Retriever Examinations

You may be enrolled in the research registry if you meet the enrollment criteria. Before any procedure is done, the doctor will obtain your medical history, perform a physical examination, and review your blood tests. Neurological exams including a test that measures the degree of disability or dependence on patients who have had a stroke [modified Rankin Score (mRS)] and a neurological examination to accurately and consistently assess the patient [National Institute of Health Stroke Scale (NIHSS)] will be done. Your physician will explain the Trevo Retriever procedure and the benefits and risks associated with this type of treatment and alternative treatments available to you.

Your participation in the registry includes data collection of the following assessments after the procedure:

24 (-6/+24) hours after the procedure the hospital staff with test how well you can move your arms and legs, talk, understand speech, and see in all directions.

At 5-7days after the procedure or when you are discharged, (whichever occurs first), you will again have a test to see how well you can move your arms and legs, talk, understand speech, and see in all directions. You will also be tested for how well you are able to perform your daily activities (i.e. bathing, dressing, and walking). A copy of your hospital bills may also be collected so that the costs of different treatments can be compared.

30 days (one month) after the procedure, you may return to see the doctor or you may receive a telephone call to see how you are doing and answer a few questions regarding your daily activities.

90 days (three months) after the procedure, you will be scheduled for a return visit with the doctor who will test how well you are able to perform daily activities and evaluate your progress. Your participation in the registry will be finished after this follow-up visit.

Alternative Procedures

Several devices have been cleared for revascularization of blocked intracranial arteries in patients with acute ischemic stroke within 8 hours of stroke onset. The alternative to participating in this data collection study is to receive routine treatment without providing access to your medical records and allowing collection of your medical information.

Voluntary Participation in the Trevo Registry

Your participation in this registry is completely voluntary. You may refuse to take part or you may withdraw from the registry at any time without penalty or loss of benefits to which you are normally entitled. The registry may be stopped by a regulatory authority or Stryker Neurovascular. Additionally, your doctor may decide to stop your participation in the registry, with or without your consent, for medical reasons. He/she will tell you in writing if they have decided to stop your participation in this registry. Your doctor will be available if you have any questions, at any time, regarding your participation in this registry.

At any time, you may withdraw your participation from the registry. After you withdraw your authorization, no further health information will be used or disclosed to the registry. Your physician, designated medical staff, the Stryker Neurovascular representative, or governmental regulatory body (e.g. FDA) will continue to have access to the data collected during your participation in the registry as well as to your future medical records and/or vital status information that may be related to the safety of the product being studied in this trial, with the stipulation that your identity and data be kept confidential and that this access would end at the closure of the registry. Contact your doctor for instructions on how to withdraw yourself from the registry.

Responsibilities

As a participant in the Trevo Registry, your responsibilities are:

- Follow the instructions of your doctor
- Take prescribed medications as instructed.

- Keep your Day 30 and Day 90 follow-up appointments. If it is necessary to miss an appointment, please contact the doctor or research staff to reschedule as soon as you know you will miss the appointment.
- Tell the doctor or research staff about any side effects, medications, doctor visits, or admissions to a hospital that you may have.
- Ask questions as you think of them.
- Tell the doctor or research staff if you change your mind about staying in the study.

Confidentiality

Your privacy is important. All information gathered in the Trevo Registry will be kept private. Your identity as a participant in this registry will remain strictly confidential.

If you consent to participate in this registry, you will be asked to sign a form that permits <Institution's Name> to use and disclose your personal information for purposes of the registry. For example, the form will permit <Institution's Name> to share your information with the registry staff, with the institutional review board and study oversight staff, and with any other people who will need access to your personal information in order to conduct the registry. The form will also permit <Institution's Name> to share your personal information with Stryker Neurovascular and with those who help the registry sponsor manage the registry.

Your personal information will usually be shared on study forms without your name, except when your name is necessary to make sure that the information on the study forms is accurate. Your name will not be reported in any publication. Only the data obtained as a result of your participation in this registry will be made public.

Because this registry involves devices and medications that are regulated by the US FDA and other regulatory agencies, these regulatory agencies may inspect records identifying you as a subject in this registry.

In addition, if your participation in this registry is for treatment or evaluation purposes, the hospital in which you are treated may ask you to sign a separate informed consent document for specific procedures or treatment, and that informed consent form may be included in the medical record of that facility. The medical record is maintained by your treating physician or hospital, as applicable, and will be subject to state and federal laws and regulations concerning confidentiality of medical records.

Duration of Participation

This research registry is expected to last up to 90 days after your procedure date. After your procedure, the research staff will ask you, or a family member, for a health check test of your daily activities at 30 and 90 days post procedure.

Compensation and Costs

You will not be paid to provide medical information for this registry. There is no cost to you for participating in this registry.

Treatment and Compensation for Injuries

Neither Stryker Neurovascular nor your doctor will provide financial assistance for illness, medical and/or other injury-related costs. Doctor <name> can provide you with information about the general liability policies of this institution to determine if compensation may be available from that source.

Additional Information

You or your legal representative will be notified in a timely manner of any new information that develops over the course of this study that may affect your willingness to participate in this study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

For Further Information

If you would wish to obtain more information regarding this registry or its risks, advantages, or medical alternatives, please contact the study doctor (investigator). You should also inform the study doctor if you have been injured or hospitalized for any reason during the registry.

Contact Information:

Investigator: _____ Study Coordinator: _____

Telephone: _____ Telephone: _____

For more information about your rights as a study subject contact:

_____

_____

By signing this Consent Form, you are agreeing to share your health information as it relates to your diagnosis and treatment of your stroke. This may include your medical exams, blood tests, x-ray and brain imaging exams prescribed by your physician. Your records may be looked at by representatives of the Stryker Neurovascular (Sponsor) and by Regulatory Agencies as required by law, such as the Food and Drug Administration (FDA). As a study participant, your brain images may be reviewed by a Core Lab who will provide an independent central assessment of your brain images. These images would only include your study ID number as a reference. Your physical exam and medical history information will be collected

and entered into a database. The results of specific tests and procedures you undergo to assess and/or treat your stroke will be entered into a database.

My signature below means that:

- I have read and understand this consent form.
- I have been informed of the purpose of the registry and was able to ask questions.
- All my questions were answered to my satisfaction.
- I have been given information on the procedure and have been informed of the potential benefits and risks involved. I have been provided with alternative treatment options available to me.
- I agree to voluntarily participate in the research registry based on the information provided.
- I agree to comply with the research registry follow-up requirements.
- A copy of this form and the HIPAA Authorization Form has been given to me.

Patient's Name (print)	Patient's Signature	Date Signed	Time Signed
Doctor's Name (print)	Doctor's Signature	Date Signed	Time Signed
Witness' Name (print)	Witness' Signature	Date Signed	Time Signed

If the patient is unable to consent complete the following,

Print Patient's name here: _____ is not able to consent because:

- ❑ Health status
- ❑ Minor less than 18 years of age

Legally Authorized Representative Name (print)	Signature	Date Signed	Time Signed

Legally Authorized Representative Relationship to Patient: _____

Interpreter and Translation Services Statement

If the language of this document is not my first language,

an interpreter and or translation services were offered and provided to me:

☐ YES ☐ NO ☐ NOT APPLICABLE

If yes (an interpreter was used),

Printed Name	Signature	Date	Time

THE SUBJECT OR HIS OR HER PERSONAL REPRESENTATIVE MUST BE PROVIDED A COPY OF THIS FORM IN ITS ENTIRETY AFTER IT HAS BEEN SIGNED.

<Insert Name of Hospital> <Insert Name of Investigator>

HIPAA Authorization for Participation in a Medical Device Study: Trevo Registry

<Institution Name>

We understand that information about you and your health is personal, and we are committed to protecting the privacy of that information. Because of this commitment, we must obtain your special authorization before we may use or disclose your protected health information (PHI) for the research purposes described in the Informed Consent Form for this study. This form provides that authorization and helps us make sure that you are properly informed of how this information will be used or disclosed. Please read the information below carefully before signing this form.

USE AND DISCLOSURE COVERED BY THIS AUTHORIZATION

Who will disclose, receive, and/or use your information?

The following person(s), class(es) of persons, and/or organization(s) may disclose, use, and/or receive your protected health information, but they may only use and disclose the information to the other parties on this list, to you or your personal representative, or as otherwise permitted or required by law:

☒ Stryker Neurovascular Corporation and its affiliated corporations and their respective employees, contractors and other agents ("Sponsor")

☒ Every research site for this study, including this Institution, and including each site's research staff and medical staff

☒ Every health care provider who provides services to you in connection with this study

☒ Any laboratories and other individuals and organizations that analyze your health information in connection with this study in accordance with the study's protocol

☒ The United States Food and Drug Administration, Medicare, Medicaid, Notified Bodies, Competent Authorities and other regulatory agencies

☒ The members and staff of the Institution's affiliated Institutional Review Board, Ethics Committee(s), Privacy Board, and all other institutional review boards or persons who watch over how the research is performed and/or monitor the safety and success of the research, including the Institution that approves this study

☒ Principal Investigator

☒ Study Coordinator

☒ Members of the Research Team, including core lab review of brain imaging tests

☒ Members of the Institution's administrative staff responsible for administering clinical trials and other research activities

What information will be used or disclosed?

The entire research record and any medical records held by the Institution and any health care provider authorized to disclose, use, or receive the information may be used and disclosed.

What could happen if you agree to this use or disclosure of your health information?

- There is the possibility that information disclosed under this authorization for the use of your personal health information may be re-disclosed and that the Federal privacy laws (laws that protect the privacy to your personal health information) may no longer protect it from being given to another person, class of persons, and/or company.

- Once information that could be used to identify you has been removed and your information is no longer identifiable (connected to your identity), the information that remains is no longer protected by this Authorization (agreement) and may be used and given by the Researchers and Sponsor to others, including for other research reasons.

- The Researchers and Sponsor have agreed that no publication or presentation of the research will reveal your identity without your separate specific written permission and authorization (agreement) [even if you revoke (take back) this Authorization (agreement)].

What rights do you have?

- You have a right to refuse to sign this authorization. While your health care outside the study, the payment for your health care, and your health care benefits will not be affected if you do not sign this form, you will not be able to participate in the research described in the informed consent form and will not receive treatment as a study participant if you do not sign this form.

- You may change your mind and cancel this agreement at any time. To cancel this agreement, you must write to: <insert name of Study Coordinator, Principal Investigator, or other responsible person or department, with full Institution Name and Address>. However, if you cancel this agreement, you may no longer be allowed to participate in the research study and may no longer receive research-related treatment. Also, even if you cancel this agreement, the information already obtained may remain a part of the research as necessary to preserve the integrity of the research study.

- You will be given a copy of this agreement after you have signed it.

When does this Authorization expire?

This authorization will never expire unless and until you revoke it.

*Please use this alternative language for **California**:*

*"*This Authorization has no expiration date, but shall expire at the end of the research study identified above".

<Insert Name of Hospital> <Insert Name of Investigator>

SPECIFIC UNDERSTANDINGS

By signing this research authorization form, you authorize the use and/or disclosure of your protected health information (PHI) described above. The purpose for the uses and disclosures you are authorizing is to conduct the research project explained to you during the informed consent process and to ensure that the information relating to that research is available to all parties who may need it for research purposes. Your information may also be used as necessary for your research-related treatment, to collect payment for your research-related treatment (when applicable), and to run the normal business operations of the Institution or other providers providing services in connection with this study.

SIGNATURE

By signing below I represent and warrant that I have authority to sign this document and authorize the use or disclosure of protected health information (PHI) and that there are no restrictions that would prevent me from authorizing the use or disclosure of this Protected Health Information (PHI).

I have read this form and all of my questions about this form have been answered.

Printed Name	Signature	Date	Time Signed

If the patient is unable to consent complete the following,

Print Patient's name: _____ is not able to consent because:

- ❑ Health status
- ❑ Minor less than 18 years of age

Legally Authorized Representative Name (print)	Signature	Date Signed	Time Signed

Legally Authorized Representative Relationship to Patient: _____

<Insert Name of Hospital>	<Insert Name of Investigator>	
Address: _____	Telephone: _____	(daytime)
_____	_____	(evening)
_____	Email: _____	

THE SUBJECT OR HIS/HER LEGALLY AUTHORIZED REPRESENTATIVE
MUST BE PROVIDED WITH A COPY OF THIS FORM AFTER IT HAS BEEN SIGNED

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↘	✔		✔			
Angiogram Procedure Information ‡***↘		✔				
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.
***See study binder for worksheets listing items to record during the procedure.
****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
↘ 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)

[See Study Binder for NIHSS Worksheet]

Reference

National Institute of Health, National Institute of Neurological Disorders and Stroke Scale. http://www.ninds.nih.gov/doctors/NIH_Stroke_Scale.pdf