SMART – A prospective, multicenter registry assessing the embolization of neurovascular lesions using the Penumbra SMART COIL® System

Protocol
CLP 10023.B

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Device Name
Penumbra SMART COIL® System

Sponsor
Penumbra, Inc.
One Penumbra Place
Alameda, CA 94502
USA

Contacts

Brooke Lawson
Clinical Project Manager
Telephone: + 1.510.995.2183
E-mail: brooke.lawson@penumbrainc.com

Amaëlle Vuillame
Director Clinical Affairs Europe
Telephone: + 33.634.30.21.12
E-mail: avuillaume@penumbrainc.com

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1. PROTOCOL SYNOPSIS

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Registry Title:	**SMART – A prospective, multicenter registry assessing the embolization of neurovascular lesions using the Penumbra SMART COIL® System**
Objective:	The primary objective of this registry is to gather post market data on the Penumbra SMART COIL® System (Smart System) in the treatment of intracranial aneurysms and other malformations.
Registry Design:	This is a prospective, multi-center registry of patients treated in accordance with the cleared indications for Smart, Penumbra Coil 400™ (PC 400), and Penumbra Occlusion Device (POD®). Data for each patient are collected in accordance with the standard of care at each participating hospital through one-year follow-up.
Patient Population:	Approximately 1,000 patients with intracranial aneurysms or other malformations treated by Smart at up to 100 centers will be enrolled.
Sample Size Justification:	Approximately 1,000 patients will be enrolled in this post market registry. Assuming an observed rate of 8.3% for the primary endpoint of re-treatment at follow-up, the sample size precision is ± 2% for this endpoint. Assuming an observed rate of 1.7% for the primary endpoint of procedural device-related serious adverse events at immediate post-procedure, the sample size precision is ± 1% for this endpoint. These precision estimates are based on binomial 95% confidence intervals. The sample size provides an adequate level of precision for these primary endpoints.
Inclusion Criteria:	Patients enrolled in this registry must sign the Informed Consent Form and be treated according to the cleared indications for Smart, PC 400, and POD, which include the embolization of: 1. Intracranial aneurysms 2. Other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae
Exclusion Criteria:	1. Life expectancy less than one year 2. Smart, PC 400, or POD account for less than 75% of total number of coils implanted 3. Patient previously enrolled in the SMART Registry 4. Participation in another clinical investigation that could confound the evaluation of the registry device
Endpoints:	1. Retreatment through follow-up 2. Procedural device-related serious adverse events 3. Ability to achieve adequate occlusion immediate post procedure 4. Number of times re-access with guidewire was required due to catheter kickout
Registry Period:	It is anticipated patient enrollment will take 3 years. All patients are to be assessed in accordance with the standard of care at each participating hospital through one year follow-up.

2. INTRODUCTION

Intracranial aneurysms are a significant health problem in the United States with an estimated 1% to 6% of the adult population harboring cerebral aneurysms.[1,2] The annual risk of rupture of an intact intracranial aneurysm is estimated to be approximately 1.9%.[2] If an intracranial aneurysm ruptures, blood leaks into the highly sensitive subarachnoid space around the brain, resulting in a subarachnoid hemorrhage (SAH). SAH is known to be a major risk factor for a stroke due to the irritation of the outer layer of the nearby blood vessels surrounding the brain. This condition is associated with a high rate of mortality; close to half of ruptured aneurysms result in death within six months.[2-4] Patients who survived the initial SAH are at significant risk of subsequent re-rupture. Various reports indicate that if left untreated, there is a re-bleeding rate of more than 50% within the first six months from initial presentation of a SAH.[4,5]

Even if an intracranial aneurysm does not rupture, it can lead to severe complications. As the aneurysm grows, it can press on nerves, put pressure on brain tissue, or interfere with other arteries or veins. Blindness, paralysis, and other morbidities often result. Thrombus can also form within the aneurysmal sac, break off, travel downstream, and cause an ischemic stroke. It has been reported that 2.2% to 23% of patients with unruptured aneurysms may eventually experience a rupture.[7,8] The International Study of Unruptured Intracranial Aneurysms evaluated the natural history of 1,937 unruptured aneurysms in 1,449 patients with a mean follow-up of 8.3 years.[8] It reported that 2.2% of these patients had a confirmed rupture during follow-up, but 66% of them were fatal. Juvela et al. reported on the long term natural history of unruptured intracranial aneurysms in a series of 142 patients.[7] With a median follow-up of 19.7 years, 23% of the patients experienced a SAH, which corresponds to an annualized rate of 1.3%. The cumulative rate of SAH tended to increase with time, with a rupture rate of 10.5% at 10 years, 23% at 20 years, and 30.3% at 30 years after diagnosis. Approximately half of the SAH patients did not survive. Thus, regardless of the rate of occurrence, fatality associated with this event is high in this cohort.[7, 8]

Prior to 1995, the traditional treatment for intracranial aneurysms was surgical clipping, in which the skull is surgically opened so metal clips can be applied to the aneurysm's neck to occlude it from the parent artery to prevent a rupture.[1] This treatment, while effective, is high risk, highly invasive, requires an extended hospital convalescence, and is technically difficult to perform in certain regions of the brain (such as the posterior circulation). Thus, this treatment modality is not a viable option for a significant number of patients, particularly during the acute phase of SAH, when the presence of cerebral edema and evolving thrombi formation render aneurysm access difficult, if not impossible.

In the early 1990's, an endovascular treatment technique for intracranial aneurysms was first introduced by Guido Guglielmi, who used electrolytically detachable platinum coils to pack and embolize the aneurysmal sac.[9, 10] The

rationale was to exclude the aneurysm from the circulation and thus reduce the risk of a rupture and SAH. The Guglielmi detachable coil (GDC) was not universally accepted at first but gained significant credibility after obtaining approval from the FDA for the intracranial aneurysm indication. Moreover, a few well-conducted, prospective, randomized studies of both ruptured and unruptured aneurysms have demonstrated that angiographic and clinical outcomes from this treatment modality were equivalent, if not better, than those obtained from surgical clipping.[6,8,11,12] Results were found to be similar for both treatments regardless of the inter-study differences in definitions for these outcome measures.[6,8,11,12] The most important landmark study was the International Subarachnoid Aneurysm Trial (ISAT) in which a total of 2,143 patients with ruptured intracranial aneurysms were randomized to either neurosurgical clipping or endovascular GDC coiling. The results showed that at one year follow-up, 30.6% of the patients treated by neurological clipping were either functionally dependent or dead as vs. 23.7% of those treated by GDC coiling, which resulted in a risk reduction rate of 22.6%. And thus, embolic coiling has now become the standard of care worldwide for endovascular occlusion for both incidental and ruptured intracranial aneurysms.

In light of the natural history of the disease, the primary focus for management of an intracranial aneurysm must be to prevent its rupture and sequelae.

The Penumbra SMART COIL® System (Smart System), a new generation of detachable coils, is the latest in Penumbra's line of embolization tools. It has recently received 510k clearance in the U.S. and CE Mark in Europe. This coil system is specifically designed to promote aneurysm embolization.

Coil technology has evolved considerably since the initial introduction of the GDC coil over 25 years ago. In recent history, coil development has mostly focused on the delivery system, or pusher technology, and detachment. The new Smart System not only addresses improvements in the delivery system, but importantly incorporates new technology into the actual coil implant itself. Smart technology enables an individual coil to become progressively softer as it is deployed, utilizes advanced materials to improve stretch resistance, and incorporates new processes to create accurate complex and helical shapes.

Current coils available to physicians have three principal levels of softness, standard, soft and extra soft. A conventional coil currently has only one level of softness, derived from using smaller platinum filaments than a standard coil to make soft and extra soft coils. The level of softness of the Smart coils is determined not only by the diameter of the platinum filament, but also by a proprietary structural element inside the coil. This unique development enables the Penumbra Smart System to become progressively softer along the length of a single individual coil as it is being deployed. For example, deployment of a standard Smart coil begins with an atraumatic soft 2D loop, becomes standard for the body of the coil, and finishes with a soft proximal end. This progressive

softness enables the coil to be densely packed into a delicate lesion while maintaining catheter position and mitigating catheter kick-back at the end of delivery, which can preclude the successful complete embolization of the lesion.

In addition, Smart uses the latest ultra high molecular weight polymers for stretch resistance, which are 3 times stronger than current stretch resistant materials such as polypropylene (found in most 10-system coils).

The Penumbra Coil 400™ (PC400) system received 510k in the U.S. and has CE Mark.

PC400 fundamentally differs from other embolic products for treatment of brain aneurysms by offering the largest outer diameter coil available. PC400 has up to four times more volume per unit length than most other embolic coils available while still maintaining a soft and compliant feel. Together, these characteristics represent the potential to improve the ability to densely fill larger aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae, thus triggering the healing process.

Penumbra Occlusion Device (POD®), was developed to address a specific clinical need to rapidly and precisely occlude a target vessel. Current options for vessel occlusion are limited. Coils designed for aneurysms are not ideally suited for vessel embolization due to their tendency to migrate with antegrade flow. Other options, such as vascular plug technology for larger vessels, require access with large diagnostic catheters or even larger bore sheaths.

POD utilizes technology that delivers both variable sizing and softness to provide a solution for rapid and precise embolization of the target vessel.
The technology achieves this range of features through the design of a distal anchoring segment, thereby immediately anchoring the device in a range of vessel diameters. The proximal segment of the POD achieves dense occlusion by packing a softer, smaller diameter segment tightly behind the anchored portion.

All three systems (Smart, PC 400, and POD) above consist of: an implantable Coil constructed of 92% Platinum and 8% Tungsten round wire, an attached detachment pusher, and a detachment handle (packaged separately). The detachment pusher is comprised of a shaft with a radiopaque positioning marker, a distal detachment tip, and a pull wire. The detachment handle is used to detach the coil implant from the detachment pusher. All three systems are designed for endovascular embolization of aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae. The intended users for this device are physicians who have received appropriate training in interventional neuroradiology.

These devices provide a comprehensive product family for the management of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae.

3. REGISTRY OVERVIEW

This is the first multicenter post market registry examining Smart and its primary objective is to gather real world experience and data on the Smart System in the treatment of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae.

3.1 Registry Design

This is a prospective, multi-center registry of patients treated in accordance with the cleared indications for the Penumbra Smart System, Penumbra Coil 400™ (PC 400), and Penumbra Occlusion Device (POD®) for intracranial aneurysms and other neurovascular abnormalities. Data for each patient are collected in accordance with the standard of care at each participating hospital through one-year follow-up.

3.2 Registry Objectives/Endpoints

This is the first multicenter post market registry examining the Penumbra Smart System. Its purpose is to gather real world experience on the Smart System in the treatment of intracranial aneurysms and other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae.

Approximately 1,000 patients with intracranial aneurysms or other malformations treated by the Penumbra Smart System, PC 400, and/or POD at up to 100 centers will be enrolled.

3.2.1 The Endpoints are:

- Retreatment through follow-up
- Procedural device-related serious adverse events at immediate post-procedure
- Ability to achieve adequate occlusion - based on investigator's adjudication of adequate occlusion given anatomical and other considerations immediate post-procedure
- Number of times re-access with guidewire was required due to catheter kickout

3.3 Registry Population

Patients enrolled in this registry must sign the informed consent form and be treated in accordance with the cleared indications outlined in the *Instructions for Use* for Smart, PC 400, and/or POD. Patients will be considered enrolled at the time of consent and procedure has begun with the intent of implanting coils.

Patients who fail to meet entry criteria pertaining to coil selection will be considered a screen fail and monitored through discharge for safety reasons.

3.3.1 Inclusion Criteria

Embolization of:

- Intracranial aneurysms
- Other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae

3.3.2 Exclusion Criteria

- Life expectancy less than one year
- Smart, PC 400, or POD account for less than 75% of total number of coils implanted
- Patient previously enrolled in the SMART Registry
- Participation in another clinical investigation that could confound the evaluation of the registry device

4. REGISTRY PROCEDURES

All registry procedures are to be conducted in accordance with the cleared indications outlined in the *Instructions for Use* for Smart, PC 400, and POD.

SCHEDULE OF ASSESSMENTS

Assessment	Admission Evaluation	Immediate Post-Procedure	Discharge	One Year Follow-Up*
History	√			
Modified Rankin Scale**	√			√
Hunt and Hess+	√			
Aneurysm Occlusion		√		√
Procedural Data Points++		√		
Adverse Events		√	√	√

* Single follow-up visit to be conducted in accordance to the standard of care at the participating hospital. Period for which to capture follow-up visit is within one year ±6 months

** Only for patients in which mRS would be captured as standard of care

+ Required for patients with SAH only

++ Proportion of SMART coils implanted, target location access attempts, radiation exposure, coiling start/end time

5. INVESTIGATOR RESPONSIBILITIES

5.1 Institutional Review Board Approval / Ethics Committee Approval

Prior to enrolling patients into the registry, the investigator will ensure that proper Institutional Review Board (IRB) / Ethics Committee (EC) approval is obtained, in accordance with applicable local state and federal laws and regulations. The IRB/EC shall approve all registry documents, including the final protocol, amendments to the protocol, and the informed consent.

5.2 Informed Consent

The investigator is responsible for ensuring that a signed informed consent is obtained according to national and state requirements prior to inclusion of patients in the registry. For patients being treated in emergent cases (i.e. ruptured aneurysm) patients will be allowed to be enrolled if they sign consent no longer than 1 calendar day after the procedure, or if a legally authorized representative signs the informed consent on the patient's behalf.

5.3 Adherence to Protocol/Amendments and Applicable Law

The investigator is responsible for ensuring that the registry is conducted according to this protocol and in accordance with the relevant aspects of EN ISO 14155:2011, Declaration of Helsinki, along with any conditions imposed by the reviewing Institutional Review Board (IRB) or Ethics Committee (EC), and all other applicable regulations.The investigator shall approve and adhere to this protocol and any amendments that arise during the course of the registry.

It is the investigator's responsibility to ensure that the staff assisting with the registry have the appropriate qualifications, are fully instructed on the registry procedures, and will respect the confidentiality statement.

5.4 Case Report Form Completion

The investigator and registry staff shall complete the electronic case report forms (eCRFs) associated with this registry. Patient numbers shall be used to identify individual patients in this registry. The eCRFs should be a complete and accurate record of patient data collected during the registry. It is the investigator's responsibility to ensure the quality of the data collected and recorded.

5.5 Reports

The investigator will be responsible for the following reports:

5.5.1 Protocol Deviation

Any deviations from the protocol identified during monitoring or through other means should be clearly documented. These include but are not limited to:

- Subject does not meet inclusion/exclusion criteria
- Incomplete or missing data
- Failure to sign informed consent
- Improperly signed or incomplete informed consent
- Delayed reporting of serious, device related, or unexpected adverse events
- Out of window visits or assessments

5.5.2 Adverse Event Reporting

Since this a post market registry, we will only be collecting Adverse Events (AEs) **related** to the procedure or device, unanticipated adverse device effects (UADE), and all Serious Adverse Events (SAEs) from the time of consent through registry exit. If an AE occurs that is not related to the procedure or device, it is not reportable under this Protocol.

5.5.2.1 Definitions

- **Adverse Event (AE)** : An ***AE*** is any undesirable clinical event occurring to a patient, during a clinical trial, whether or not it is considered related to the device. This includes a change in a patient's condition or laboratory results which has or could have a deleterious effect on the patient's health or well-being.

- **Adverse Device Effect (ADE):** An adverse device effect related to registry device(s).

- **Serious Adverse Event (SAE):** A ***SAE*** is an event that:
  a. Led to death
  b. Led to a serious deterioration in the health of the patient that:
     - Resulted in life-threatening illness or injury
     - Resulted in permanent impairment of a body structure or a body function
     - Required in-patient hospitalization or prolongation of existing hospitalization
     - Resulted in medical or surgical intervention to arrest permanent impairment to body structure or a body function
     - Led to fetal distress, fetal death or a congenital abnormality or birth defect

- **Unanticipated Adverse Device Event (UADE):** An event that has an Adverse Device Effect, the specificity or severity of which is

not consistent with the with the risk information described in the *Instruction for Use* or the clinical protocol.

5.5.2.2 Relationship to the Registry Device

An AE is considered to be device-related when it is reasonable to believe that the event may have been caused by or is related to the device. Following definitions will be used to assess the relationship of the adverse event to the use of registry device. Any grading for relatedness other than 'unrelated' will be considered device related.

- **Definite:** The temporal sequence is relevant and the event abates upon device application completion/removal, or reappearance of the event on repeat device application
- **Probable:** The temporal sequence is relevant or the AE abates upon device application completion/removal or the AE cannot be reasonably explained by the subject's condition or comorbidities. The AE is related or most likely associated with the device
- **Possible:** The temporal sequence between the device and the AE is such that the relationship is not unlikely or there is no contradicting evidence that can reasonably explain the registry subject's condition. There is a possibility of a relationship between the AE and the device
- **Unrelated:** The AE is not associated with the device. There is no relation between the AE and the device

Similar grading will be used for assessing the relationship to procedure.

5.5.2.3 Adverse Event Severity

For the purposes of this trial, the investigator will use the following definitions to rate the severity of each adverse event**.**

- **Mild:** Awareness of a sign or symptom that does not interfere with the patient's usual activity or is transient, resolves without treatment and with no sequelae
- **Moderate:** interferes with routine activity and/or requires symptomatic therapy
- **Severe:** Severe discomfort and significant impact on the subject's ability to perform routine activities despite symptomatic therapy

Minimum requirements of data to be recorded are: type of event, duration of event (start through end), severity, seriousness, action taken, outcome and, if appropriate, causality.

The Investigator is required to report any device or procedure related AE, UADE and/or SAEs to the Sponsor or its designee as soon as possible, but no later than 24 hours after the event is known. All serious adverse events or serious device effects must document an explanation of any medical treatment administered. The form must be completed and submitted to the Sponsor or its designee within five working days.

An event need not be reported as a SAE if it represents only a relapse or an expected change or progression of the condition that was the cause of treatment without any other symptoms and signs than those present before treatment. This type of event is considered an AE, and may not be reportable.

When appropriate, the IRB/EC shall be informed by the investigator about serious adverse events and adverse device effects associated with the use of the product, and Penumbra is responsible for informing the Health Authorities and other investigators of such events as appropriate.

5.6 Withdrawal of Approval

The investigator shall report to Penumbra immediately if, for any reason, the approval to conduct the investigation is withdrawn by the IRB/EC. The report will include a complete description of the reason(s) for which approval was withdrawn. The investigator shall submit all reports in a timely manner.

5.7 Records Retention

The investigator shall maintain the records associated with this registry for a period of at least two years after the date on which the investigation is completed. These records include the following:

- Correspondence with the Sponsor or designee, the medical monitor, and other investigators.
- Patient records, including informed consent forms, copies of all completed eCRFs, and supporting documents.
- Current registry protocol with dates and details of reasons for any deviations from the protocol that could affect the scientific quality of the registry or the rights, safety, or welfare of the patients.
- Reports of any serious adverse event or adverse device effects.
- A copy of all approvals related to the clinical investigation.
- The approved, blank, informed consent form.
- Certification that the investigational plan has been approved by the IRB/EC.
- Signed investigator agreements and current signed and dated *curriculum vitae* of the registry investigator and all participating investigators.

6. SPONSOR RESPONSIBILITIES

6.1 Training

During registry initiation, the Sponsor will train the investigator and registry staff on the protocol as well as the eCRFs.

6.2 Investigator List

The Sponsor shall keep a list of the names, addresses, and professional positions of the investigators for the registry.

6.3 Adverse Event Reporting

The Sponsor shall evaluate adverse event reports received from the registry sites and those found during data monitoring and shall report them to the regulatory bodies and other investigational sites as appropriate.

6.4 Data Monitoring

Sponsor will be utilizing both centralized and on-site monitoring during the trial. Standardized eCRFs will be used for queries and query resolution. A Penumbra employee or designate will conduct the following site visits:

6.4.1 Site Initiation Visit

This is conducted on site or remotely to train the registry staff on registry requirements, and other relevant training.

6.4.2 Interim Monitoring Visit

Conducted as needed to ensure the registry site is operating in compliance with this protocol, and completing the eCRFs. Clinical monitoring will include review and resolution of missing or inconsistent data and source document checks to ensure the accuracy of the reported data. eCRFs for all enrolled patients will be made available to the Sponsor for review as agreed with the investigator. The Sponsor will evaluate and summarize the results of each site visit in written reports, identifying repeated data problems with any investigator and specifying recommendations for resolution of noted deficiencies. To facilitate this monitoring, certain source documents may be requested. These may include, but are not limited to, patient informed consent, history and physical, operative report, imaging reports, and discharge summary.

6.4.3 Registry Close-Out Visit

This visit is conducted at the termination of the registry to resolve any outstanding data queries and reconcile trial documents.

6.5 Data Management

All registry data will be entered into an electronic data capture (EDC) system provided by a vendor. Registry personnel will have individual login and password to access the clinical registry information based upon each individual's roles and responsibilities. For data security, the system operates within the Secure Socket Layer (SSL) 256-bit encryption protocol. This application is designed to support compliance with the appropriate regulations and guidance for industry.

Data entry will be performed at the investigational sites. Standardized eCRFs will be provided for use at all investigational sites. Investigators are responsible for completion and timely submission of the data to Penumbra, Inc. This EDC system requires no on-site software installation or specific hardware to operate. Investigators, clinical coordinators, data managers, and Penumbra clinical personnel access project information and registry data centrally via a Web browser. Incoming data are to be reviewed for quality and consistency before being locked for data export. Questions or problems with submitted data will be addressed with the principal investigator or designee via an electronic querying system, or through direct contact.

All hard copy forms and data files will be secured to ensure confidentiality. Investigators are required to maintain source documents required by the protocol, including laboratory results, patient report forms, supporting medical records, and Informed Consent Forms. The source documents will be used during the regular monitoring visits to verify information submitted on the eCRFs.

7. CONTACT INFORMATION

The address of Penumbra Incorporated is:

Penumbra, Inc.
One Penumbra Place
Alameda, CA 94502
Tel. (510) 748-3200
Fax (510) 814-8305

Key contacts for the SMART registry include:

Brooke Lawson, MS CCRA	Clinical Project Manager	+1.510.995.2183
Melissa Dillman, RN	Director, Clinical Operations	+1.317.490.4422
Michaella Corso	Director, Clinical Affairs	+1.510.995.2079
Amaëlle Vuillaume	Director, Clinical Affairs Europe	+ 33.634.30.21.12

8. ETHICAL REQUIREMENTS

8.1 IRB/EC Approval

The investigator is responsible for ensuring that the registry is conducted according to any conditions imposed by the reviewing Institutional Review Board (IRB) or Ethics Committee (EC), and all other applicable regulations. It is the responsibility of the investigator to obtain approval of the registry protocol from the IRB/EC and to keep the IRB/EC informed of any unexpected serious adverse events, serious adverse device effects, and amendments to the protocol, as applicable. All correspondence with the IRB/EC should be filed by the investigator and copies sent to the Sponsor or its designee.

8.2 Patient Information and Consent

It is the responsibility of the investigator to give each patient full and adequate verbal and written information regarding the objective and procedure of the registry and the possible risks involved and to obtain signed informed consent from all patients prior to inclusion in the registry unless the patient's health condition does not allow informed consent, in which case the state and national procedures will be applied. For patients being treated in emergent cases (i.e. ruptured aneurysm), patients will be allowed to be enrolled if they sign consent no longer than 1 calendar day after the procedure or if a legally authorized representative signs the informed consent form on the patient's behalf. The original, signed consent is filed with the patient registry records, and a copy is provided to the patient or legally authorized representative.

8.3 Patient Data Protection

The patients will be identified in the eCRFs with a unique patient identifier. Only the investigator will have access to individual patient data, as will the Sponsor or its designee for monitoring purposes only. Furthermore, the patients should be informed about the possibility of inspection of relevant parts of the hospital records, including angiograms and other imaging scans, by the Sponsor or other health authorities, including the FDA.

9. STATISTICAL PROCEDURES

9.1 Sample Size Justification

Approximately 1,000 patients will be enrolled in this post market registry. Assuming an observed rate of 8.3% for the endpoint of re-treatment at follow-up, the sample size precision is greater than ± 2% for this endpoint (95% CI: 6.6% to 10.0%).[14-21] Assuming an observed rate of 1.7% for the primary endpoint of procedural device-related serious adverse events at immediate post-procedure

(data on file at sponsor), the sample size precision is greater than ± 1% for this endpoint (95% CI: 0.93% to 2.5%). These precision estimates are based on binomial 95% confidence intervals. Hence, the sample size provides an adequate level of precision for these primary endpoints.

9.2 General Statistical Methods

This registry is a single-treatment design. Hence, descriptive statistics will provide a basis for the majority of the analyses with a 95% two-sided confidence interval presented. For binary outcomes, the 95% two-sided confidence intervals will be calculated using binomial intervals. For numeric measures, a confidence bound for the mean or mean change from admission will be constructed.

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, effectiveness variables, and safety variables, as appropriate. Continuous variables will be summarized with descriptive statistics (n, mean, standard deviation, range, and median). Frequency counts and percentage of patients within each category will be provided for categorical data.

Results collected at multiple visits will be summarized at each visit for which they are collected. Summaries for all measures will include all observed data for each visit.

9.3 Safety

Tabulations of adverse events will be presented with descriptive statistics at immediate post procedure and follow-up visits. Adverse event incidence rates will be summarized by category and seriousness of the adverse event. Events will also be reported by relationship to the device.

10. PUBLICATION OF INFORMATION

The results of this registry may be offered for publication and/or presentation. The investigators and the Sponsor shall collaborate in the writing of the registry to ensure accuracy. The investigator agrees to use this data only in connection with this registry and will not use it for other purposes without written permission from the Sponsor.

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