AZIYO®
BIOLOGICS

CLINICAL PROTOCOL
11-PR-1021
Rev. B

Prepared/Approved

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CORMATRIX® ECM® FOR CAROTID REPAIR FOLLOWING ENDARTERECTOMY REGISTRY

PROTOCOL NUMBER: 11-PR-1021
REVISION: B

SPONSOR:
CORMATRIX CARDIOVASCULAR, INC.
286 S. MAIN ST., SUITE 200
ALPHARETTA, GA 30009

DATE: FEBRUARY 7, 2018

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DATE: FEBRUARY 7, 2018

Robert Matheny, M.D., Chief Scientific Officer, CorMatrix Cardiovascular, Inc.

Signature: _____ **Date:** _____

Investigator Signature Page

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Site Name: _____

Print Investigator Name: _____

Investigator Signature: _____ **Date:** _____

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ATTACHMENT 3: DRAFT CASE REPORT FORMS

EXECUTIVE SUMMARY

TITLE OF REGISTRY:	CorMatrix® ECM® for Carotid Repair Following Endarterectomy Registry
PROTOCOL NUMBER:	11-PR-1021
OBJECTIVES:	To capture and assess device performance data from subjects undergoing patch angioplasty of the carotid artery following carotid endarterectomy using the CorMatrix ECM for Carotid Repair per its FDA cleared Indications for Use. To provide an ongoing post-market surveillance mechanism to document clinical outcomes on the use of the CorMatrix ECM for Carotid Repair.
REGISTRY DESIGN:	A multi-center, prospective, single-arm, post-market, observational registry of subjects receiving the CorMatrix ECM for Repair for patch angioplasty following carotid endarterectomy (CEA) procedures.
ENROLLMENT:	Up to 230 subjects may be enrolled from up to ten U.S. clinical sites.
INCLUSION CRITERIA:	Subjects must be undergoing carotid endarterectomy with patch angioplasty closure. Subject's operative surgeon intends to use CorMatrix ECM as the patch material for closure of the carotid artery per its FDA cleared Indications for Use. The subject must possess the ability to provide written Informed Consent. The subject must express an understanding and willingness to fulfill all of the expected requirements of this clinical protocol.
EXCLUSION CRITERIA:	Subjects with a known sensitivity to porcine material.
REGISTRY PROCEDURES:	Baseline clinical evaluation and standard follow-up evaluations, including carotid duplex imaging, at 1 to 3-months, 6-months, 12-months, and 24-months postprocedure. Follow-up data will be collected and entered by site personnel in SUGAR COMMUNITY EDITION, electronic data capture system.
OUTCOME MEASURES:	Carotid procedure and device related adverse events to determine device performance data will be collected.
STATISTICAL ANALYSIS:	Descriptive analyses will include overall subject characteristics and outcomes.

	REGISTRY CONTACTS
SPONSOR	CorMatrix Cardiovascular, Inc. Rhonda Van Genderen 286 S. Main St., Suite 200 Alpharetta, GA 30009 Cell: 715-441-5411 Email: rvangenderen@cormatrix.com FAX: 1-800-861-8179 Telephone: 678-566-2628

REVISION HISTORY	
REVISION	**DESCRIPTION OF CHANGE**
REVISION A JANUARY 24, 2012	INITIAL RELEASE
REVISION B FEBRUARY 7, 2018	PROVIDED INFORMATION ON ELECTRONIC DATA CAPTURE

1.0 INTRODUCTION

1.1 BACKGROUND

Ischemic stroke caused by carotid artery atherosclerosis constitutes major morbidity, mortality, and health care expenditure. Carotid endarterectomy (CEA) is performed to remove atherosclerotic plaque and reduce stroke risk. CEA has been studied extensively within the context of the patient's symptomatic status and degree of carotid stenosis, or narrowing. It has been shown to reduce longer-term risks of stroke in patients without neurologic symptoms and those with prior transient ischemic attacks (TIA) and non-disabling stroke (ACAS/ECST/NASCET/ACST) who have hemodynamically significant carotid stenosis. As such a studied procedure, technical aspects of its performance have been scrutinized. After the endarterectomy portion of the procedure is performed, the arteriotomy must be closed. This can be done by primary closure using suture to reapproximate the longitudinal artery opening, or with a patch. This is known as "patch angioplasty." Patch angioplasty has evolved over time, and it is now widely accepted that use of a patch for closure significantly reduces the risks of carotid restenosis, stroke, and death.[1] There are several materials, which have been utilized for patch closure after CEA. These include autogenous saphenous vein, cervical veins, glutaraldehyde-treated bovine pericardium, and synthetic materials (i.e., ePTFE, Dacron, etc.). However, currently available synthetic or chemically treated patch materials may induce scar tissue formation leading to restenosis and can lead to a higher risk of infection.[2] The CorMatrix ECM for Carotid Repair is an attractive vascular patch material due to its ability to be remodeled into healthy native tissue.

1.2 DEVICE DESCRIPTION

The CorMatrix ECM for Carotid Repair is an acellular, natural collagen construct, derived from the porcine small intestine submucosa that has demonstrated the ability to provide a scaffold for cells for remodeling various tissues following implantation into subjects.

The CorMatrix ECM for Carotid Repair is supplied in a six-ply sheet, which can be cut to size as the physician deems necessary for the specific procedure to be performed. The CorMatrix ECM for Carotid Repair is provided in a lyophilized, sterile state and is for single use only.

1.3 REGULATORY STATUS

CorMatrix Cardiovascular, Inc. received U.S. FDA 510(k) premarket

[1] Awad IA and Little JR. Patch angioplasty in carotid endarterectomy. Advantages, concerns, and controversies. *Stroke* 1989;20;417-22.

[2] Bond R et al. Systematic review of randomized controlled trials of patch angioplasty versus primary closure and different types of patch materials during carotid endarterectomy. *J Vasc Surg* 2004;40:1126-35.

clearance (K111187) for the CorMatrix ECM for Carotid Repair on July 26, 2011.

1.4 INDICATIONS FOR USE

The CorMatrix ECM for Carotid Repair is intended for use as a patch material for vascular reconstruction and repair of the carotid artery, including patch closure following carotid endarterectomy and suture line buttressing.

2.0 REGISTRY OBJECTIVES

The objective of this registry is to capture and assess device performance data from subjects undergoing patch angioplasty of the carotid artery following carotid endarterectomy using the CorMatrix ECM for Carotid Repair per its FDA cleared Indications for Use. This registry provides an ongoing post-market surveillance mechanism to document clinical outcomes on the use of the CorMatrix ECM for Carotid Repair.

3.0 REGISTRY DESIGN

This is a multi-center, prospective, single-arm, post-market, observational registry of subjects receiving the CorMatrix ECM for Carotid Repair for patch angioplasty following carotid endarterectomy procedures.

This post-market registry may involve up to ten U.S. clinical sites and up to 230 subjects. Data will be collected through the 24-month follow-up. The data may also be used for publications.

3.1 OUTCOME MEASURES

3.1.1 Performance: Observe the performance and clinical outcome of the CorMatrix ECM for Carotid Repair for patch angioplasty following carotid endarterectomy. Collected data will include both carotid procedure and device related adverse events to determine device performance data.

3.2 SAMPLE SIZE

Up to 230 subjects may be enrolled in this registry.

3.3 REGISTRY DURATION/FOLLOW-UP

All subjects enrolled in this registry will be evaluated preoperatively and followed from their treatment date through 24-months postprocedure. Subjects will have a baseline standard clinical evaluation and standard follow-up evaluations, including carotid duplex imaging, at 1 to 3-months, 6-months, 12-months, and 24-months postprocedure. If intraoperative completion duplex or other imaging (i.e., CTA, MRA, arteriography) is performed, data should be collected, but this is not mandatory.

3.4 REGISTRY POPULATION AND ELIGIBILITY CRITERIA

Subjects must meet the following requirements in order to be eligible for enrollment in the registry:

3.4.1 Inclusion Criteria

All subjects are required to meet the following inclusion criteria in order to be considered eligible for participation in this registry:

- Subjects must be undergoing carotid endarterectomy with patch angioplasty closure.
- Subject's operative surgeon intends to use CorMatrix ECM as the patch material for closure of the carotid artery per its FDA cleared Indications for Use.
- The subject must possess the ability to provide written Informed Consent.
- The subject must express an understanding and willingness to fulfill all of the expected requirements of this clinical protocol.

3.4.2 Exclusion Criteria

Subjects will be excluded from participating in this registry if the following exclusion criterion is met:

- Known sensitivities to porcine material

3.5 PROCEDURAL OVERVIEW

After a subject has undergone the preoperative evaluation, has been determined to be eligible for the registry and signed an Informed Consent Form, he or she will be considered enrolled in the registry. After enrollment, the subject will undergo a standard carotid interventional procedure including carotid endarterectomy. The subject's carotid arteriotomy site will be closed using the CorMatrix ECM for Carotid Repair. The surgeon will implant the CorMatrix ECM for Carotid Repair according to the FDA cleared Instructions for Use.

3.6 REGISTRY SITES

Up to ten U.S. clinical sites may participate. Sites will be selected due to ability to provide expertise in carotid endarterectomy and carotid duplex imaging.

3.7 INSTITUTIONAL REVIEW BOARD APPROVALS

Before any subject can be enrolled in this registry, the Institutional Review Board (IRB) for the specific institution must approve the protocol and the Informed Consent Form to be used at that site. A subject cannot be asked

to sign the Informed Consent Form until the registry has been fully approved by the institution's IRB. The Sponsor will require a copy of any IRB correspondence, as well as the final approval letter and the final approved Informed Consent Form, from each IRB.

3.8 REGISTRY CONDUCT

This registry will be performed in accordance with Title 21 Code of Federal Regulations Parts 50 and 56 and other relevant FDA regulations and the relevant sections of the ICH Guidelines for Good Clinical Practices.

The principles of the Declaration of Helsinki have been addressed in the design of the registry, consideration of the risk and benefits to the subjects, selection of the site and Investigators to conduct the registry, measures taken to protect the health and rights of the human subjects, and registration of the registry in a publicly accessible database.

4.0 SUBJECT ENROLLMENT INFORMATION

4.1 INFORMED CONSENT

Subjects cannot be asked to sign the Informed Consent Form until the registry has been fully approved by the respective institution's IRB and the Sponsor has received and reviewed the specific IRB approved Informed Consent Form. When the Investigator has determined the eligibility of a specific subject to enter the registry, the Informed Consent Form must be completed. The Informed Consent Form must be read by the subject, the subject's questions answered and the form signed and dated by the subject, before the surgical procedure can be performed. All subjects are to receive copies of their Informed Consent Form.

4.2 SURGEON TRAINING

Surgeons will be trained prior to subject enrollment by CorMatrix personnel according to the FDA cleared CorMatrix ECM for Carotid Repair Instructions for Use.

4.3 COVERAGE OF EXPENSES

Subjects will not be reimbursed or compensated for participating in the registry; the procedure will be billed to medical insurance as per standard procedure.

4.4 CONFIDENTIALITY

Confidentiality of subjects will be maintained throughout the registry. A unique identification code will be assigned to each subject participating in this registry. Any data that may be published in abstracts, scientific journals, or presented at medical meetings will reference a unique subject code and will not reveal the subject's identity. The Sponsor will make

every reasonable effort to protect the confidentiality of the subjects participating in the registry.

5.0 DATA COLLECTION PROCEDURES

5.1 PREOPERATIVE EVALUATION

The following information will be collected for each subject: demographics, risk factors, preoperative medications (anti-platelets, anti-coagulants, anti-arrhythmics, anti-hypertensives, betablockers, and statins) taken within approximately 3 months prior to the procedure and verification that the subject meets inclusion/exclusion criteria specified in the protocol. A carotid duplex imaging or approved testing is required preoperatively (within 60 days of the procedure) to measure the percentage of carotid artery stenosis.

5.2 OPERATIVE EVALUATION

The carotid endarterectomy should be performed per the surgeon and institution's standard CEA procedures. Specific data on the CEA procedure as well as the CorMatrix ECM will be collected. Also, carotid procedure and/or device related adverse events will be documented on appropriate CRFs in SUGAR COMMUNITY EDITION, electronic data capture system.

5.3 POSTOPERATIVE EVALUATION

Postoperative data from the end of the CEA procedure until the subject is discharged from the hospital will be collected. Medications (anti-platelets, anti-coagulants, anti-arrhythmics, anti-hypertensives, betablockers, and statins) and carotid procedure and/or device related adverse events will be documented on appropriate CRFs in SUGAR COMMUNITY EDITION, electronic data capture system.

5.4 1 TO 3-MONTH FOLLOW-UP EVALUATION

Subjects will have a follow-up evaluation at 1 to 3 months after the carotid procedure. Information will be collected regarding the subject's health status, medications (anti-platelets, anti-coagulants, anti-arrhythmics, anti-hypertensives, betablockers, and statins) and the occurrence of any carotid and/or device related adverse events. A carotid duplex imaging or approved testing is required and the data will be collected on appropriate CRFs in SUGAR COMMUNITY EDITION, electronic data capture system. Results of any additional anatomic imaging performed should be recorded.

5.5 6-MONTH FOLLOW-UP EVALUATION (± 1 MONTH)

Subjects will have a follow-up evaluation 6 months (± 1 month) after the carotid procedure. Information will be collected regarding the subject's health status, medications (anti-platelets, anti-coagulants, anti-arrhythmics, anti-hypertensives, betablockers, and statins) and the occurrence of any carotid and/or device related adverse events. A carotid duplex imaging or approved testing is required and the data will be collected on appropriate CRFs in SUGAR COMMUNITY EDITION, electronic data capture system. Results of any additional anatomic imaging performed should be recorded.

5.6 12-MONTH FOLLOW-UP EVALUATION (± 1 MONTH)

Subjects will have a follow-up evaluation 12 months (± 1 month) after the carotid procedure. Information will be collected regarding the subject's health status, medications (anti-platelets, anti-coagulants, anti-arrhythmics, anti-hypertensives, betablockers, and statins) and the occurrence of any carotid and/or device related adverse events. A carotid duplex imaging or approved testing is required and the data will be collected on appropriate CRFs in SUGAR COMMUNITY EDITION, electronic data capture system. Results of any additional anatomic imaging performed should be recorded.

5.7 24-MONTH FOLLOW-UP EVALUATION (± 1 MONTH)

Subjects will have a follow-up evaluation 24 months (± 1 month) after the carotid procedure. Information will be collected regarding the subject's health status, medications (anti-platelets, anti-coagulants, anti-arrhythmics, anti-hypertensives, betablockers, and statins) and the occurrence of any carotid and/or device related adverse events. A carotid duplex imaging or approved testing is required and the data will be collected on appropriate CRFs in SUGAR COMMUNITY EDITION, electronic data capture system. Results of any additional anatomic imaging performed should be recorded.

5.8 REGISTRY EXIT

Subjects will be exited from the registry following their scheduled 24-month follow-up evaluation, or earlier if the subject withdraws from the registry, or his/her participation is discontinued by the Investigator, or death. The date each subject completed the registry per this protocol, or if not, then the date the subject exited from the registry and the primary reason should be recorded. Any subject who experiences a serious carotid and/or device related adverse event that is ongoing at the time of exit will be followed by the physician until the adverse event is resolved or the subject is medically stable in the opinion of the Investigator.

5.9 DISCONTINUED SUBJECTS

Subjects are considered enrolled once they have signed the informed consent form. There are three categories of discontinued subjects: those who withdraw from the registry prior to any activities related to the treatment procedure; those in whom implantation of the CorMatrix ECM for Carotid Repair does not occur due to clinical concerns at the time of operation; and those who elect to withdraw from the registry after implantation of the CorMatrix ECM device. Discontinued subjects will be followed by the physician until they are considered to be medically stable.

5.10 SUBJECTS LOST TO FOLLOW-UP

If the Investigator or study coordinator has attempted to contact a subject at least three times within 60 days and received no response, the subject may be considered lost to follow-up. The Investigator or study coordinator will document the minimum of three attempts to contact the subject, including sending a certified letter, and contacting the Sponsor, prior to terminating the subject from the registry.

6.0 REPORTING OF ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

6.1 DEFINITIONS

An "Adverse Event" (AE) is any clinical finding that is an undesired or pathological change in a registry subject as indicated by signs, symptoms, illnesses and events that develop or worsen in severity in association with the registry whether or not thought to be related to the device or procedure. Adverse events include current illness, injuries, side effects, toxicities, allergic reactions, or events that occur or worsen during the course of a clinical study. This registry will only collect carotid procedure and device related adverse events as well as any carotid related clinical findings.

Adverse Events will be classified as Serious Adverse Events (SAEs) if the event:

- is life threatening (even if temporary in nature) or fatal;
- results in permanent impairment of a body function or permanent damage to a body structure;
- requires medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure; or
- requires or prolongs hospitalization.

Once a clinical finding is noted, and the finding is classified as an AE or SAE, the relationship to the device will be classified as follows:

- Not Related: The event is due to an underlying or concurrent illness or effect of another device, drug or intervention and is not related to the use of the registry device.

- Possible: The event has a strong temporal relationship to the use of the registry device, and an alternative etiology is equally or less likely.
- Probable: The event has a strong temporal relationship to the use of the registry device, and another etiology is unlikely or significantly less likely.
- Definite: An event that can only be attributed to the use of the registry device.

If a SAE is determined to be probably or definitely related to the device and has not been previously anticipated, the clinical finding would be classified as an unanticipated adverse device effect (UADE). An UADE is defined as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects."

SAEs that are determined to be probably or definitely related to the study device are referred to as device related serious adverse events (DRSAEs).

The protocol definitions for "device failure" and "device malfunction" and "technical observation" are provided below:

- Device Failure: A device has failed if it does not perform according to the Instructions for Use or other labeling provided with the device and, as a result, negatively impacts the treatment when used according to this protocol.
- Device Malfunction: A device malfunction is an unexpected change to the device that is not contradictory to the labeling and may or may not affect the performance of the device.
- Technical Observation: Malfunction or complaint with a medical device that has the potential to, but may or may not, result in a negative clinical consequence to the subject.

Note: A device failure or device malfunction is considered to be a DRSAE if it causes or contributes to a SAE.

6.2 REPORTING OF ADVERSE EVENTS

Carotid procedure and device related adverse events are to be completed at any point from the time the subject is enrolled to the time of exit from the registry. Adverse events are to include carotid procedure and device related adverse events as well as any carotid related clinical findings.

Registry subjects will be instructed to immediately report to the Investigator any carotid related unusual signs or symptoms. The

Investigator will take whatever means are necessary to treat the subject, should an adverse event occur. First consideration will be given to the welfare of the subject rather than the successful completion of the registry. All subjects experiencing a carotid procedure and/or device related adverse event will be followed until their clinical outcome is determined, if at all possible, or until completion of the last follow-up visit, whichever occurs later.

All carotid procedure and/or device related findings must be recorded on the appropriate CRF in SUGAR COMMUNITY EDITION, electronic data capture system. A description of the finding, including the start date, resolution date, action taken, and the outcome should be provided, along with the Investigator's assessment of the relationship between the finding and the device. Subjects' complaints of any carotid related symptoms that are outside the normal pattern for the illness treated should be considered AEs.

All carotid procedure and/or device related AE's shall be followed until the event is resolved or determined by the Investigator to be stable. The investigational site will provide relevant follow-up information to the Sponsor upon request.

All SAEs and UADEs must be immediately reported to the Sponsor, CorMatrix Cardiovascular, via telephone or e-mail within 24 hours of the Investigator becoming aware of the event. A completed "Serious Adverse Event" form must be faxed or express mailed to the Sponsor within five working days of the event. The minimum required data to be recorded for an SAE includes: date of event, type of event, actions taken, outcome and, if appropriate, causality and possible relationship to the device(s) used in this registry. In the case of a DRSAE, when possible, the device involved in the failure or malfunction is to be made available to the Sponsor for analysis.

If a serious adverse event is being reported after normal working hours, the Investigator will leave a voice message at one of the following telephone numbers with accompanying report of the adverse event sent to the fax number(s) below:

Sponsor:
CorMatrix Cardiovascular, Inc.
Rhonda Van Genderen
286 S. Main St., Suite 200
Alpharetta, GA 30009

Cell: 715-441-5411
Email: rvangenderen@cormatrix.com
FAX: 1-800-861-8179
Telephone: 678-566-2628

The IRB will be notified of serious adverse events per the specific IRB's reporting requirements. The IRB will be informed if, in the opinion of the Sponsor or the Investigator, the serious adverse event is likely to affect the safety of the subjects or the conduct of this registry.

Follow-up reports will be filed using the Adverse Event CRF in SUGAR COMMUNITY EDITION, electronic data capture system as new information is available or there is a change in the subject's condition.

7.0 RISK/BENEFIT ASSESSMENT

7.1 RISKS TO THE SUBJECT

The possible risks associated with the use of the CorMatrix ECM for Carotid Repair for patch angioplasty after CEA are similar to the risks associated with other patch materials for reconstruction or repair of the carotid artery. Risks associated with the use of the CorMatrix ECM for Carotid Repair include:

- Acute or chronic inflammation (Initial application of the CorMatrix ECM may be associated with transient, mild, localized inflammation)
- Allergic reaction
- Bleeding
- Embolization of ECM
- Infection
- Patch dehiscence
- Pseudoaneurysm
- Recurrent stenosis
- Stroke
- Thrombosis
- Vessel occlusion

The known precautions and warnings are listed in the IFU, included as Attachment 2.

7.2 BENEFITS TO THE SUBJECT

The benefits of the CorMatrix ECM for Carotid Repair used for patch angioplasty after CEA have not been established by previous clinical studies.

Subjects participating in this registry may not receive immediate benefit; however, feedback from this registry will provide valuable information that may benefit subjects in the future.

8.0 INVESTIGATOR RESPONSIBILITIES, RECORDS AND REPORTS

8.1 INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for ensuring that this registry is conducted according to this protocol and that the signed Informed Consent Form is obtained from each subject prior to their inclusion in this registry.

It is the Investigator's responsibility to ensure that all staff assisting with this registry have the appropriate qualifications and are fully instructed on the registry procedures and respect subject confidentiality, as specified in the Investigator Agreement and Financial Disclosure. All participating Investigators are required to sign an Investigator Agreement and Financial Disclosure form prior to their participation.

The Investigator is responsible for ensuring that the conduct of the registry conforms to the IRB requirements and provides all necessary communication with the IRB including, but not limited to, annual study reports and required adverse event notifications.

8.2 INVESTIGATOR RECORDS

Source documentation and standardized Case Report Forms (CRFs) in SUGAR COMMUNITY EDITION, electronic data capture system will be used to collect complete and accurate records of the clinical data from the registry according to the Good Clinical Practices (GCP) requirements. The Investigator is responsible for collecting and accurately recording the data generated for this registry.

The Investigator is responsible for ensuring the maintenance of complete, accurate and current records including the following materials:

- All correspondence with the Sponsor and the IRB;
- Subject records, including signed Informed Consent Forms for all enrolled subjects, and all supporting source documents (laboratory reports and reports of diagnostic tests, medical records, etc.) and operative records for each subject;
- The representative copy of the IFU provided with the CorMatrix ECM for Carotid Repair utilized in this registry;
- A copy of the approved protocol for this registry and all subsequent revisions to the protocol;
- A description of any protocol deviation(s) and the justification for the deviation(s);
- Copies of carotid procedure or device related adverse events, device failure/malfunction or Medical Device Reports (MDR) submitted; and
- A copy of the approval letter from the respective Investigational Review Board (IRB), with the names of the participating members of the IRB, the approved informed consent (and any subsequent

revisions) and any specific IRB follow-up or reporting requirements to be addressed during the registry.

8.3 INVESTIGATOR REPORT

The Investigator will be responsible for providing the following reports to the Sponsor for this registry:

8.3.1 Serious Adverse Event

Serious Adverse Events are defined in Section 6.1, and the required reporting timeline and appropriate contacts are outlined in Section 6.2. The Investigator is responsible for reporting all events within the designated timeline and for maintaining initial reports and any follow-up reports that may be completed during the registry. All follow-up reports must also be sent to the Sponsor within five working days of the follow-up report being necessary due to new information or a change in the subject's status.

8.3.2 Withdrawal of Approval

If the IRB withdraws the approval to conduct the registry for any reason, the Investigator should notify the Sponsor as soon as possible and no later than five working days after the withdrawal of the approval.

8.3.3 Deviations from the Investigational Plan

The Investigator must notify the Sponsor and the reviewing IRB of any deviation from the Investigational Plan to protect the life or physical well being of a subject in the case of an emergency. This notice must occur as soon as possible, but in no case longer than five working days after the deviation has occurred. Subjects who do not meet the inclusion/exclusion criteria for the registry may not be enrolled as a deviation; any deviations from the enrollment criteria must receive prior approval from the Sponsor and IRB. Subject visits outside of window will not require a five day notification, but should be reported promptly as a deviation.

8.3.4 Use of Information and Publication

It is intended that the results of the registry may be published in the scientific literature and/or presented at scientific meetings (without disclosing the identity of the subjects in the written data or photographs). Results may also be used in submissions to regulatory authorities. Specific information regarding confidential information, and the collaboration and prior review of any planned publication activities (including presentations) is covered in the separate documentation between the Sponsor and Investigator.

9.0 MONITORING

Study monitors qualified by training and experience, will be responsible for monitoring and overseeing the conduct of the registry. The study monitors may evaluate compliance with the protocol, FDA regulations, any specific recommendations made by the site's IRB and the signed Investigator Agreement. Phone contacts and site visits may be conducted to ensure that the protocol is being followed and that any protocol deviations are properly documented. The Investigator will make available to the study monitor for review all Informed Consent Forms, all completed CRFs in SUGAR COMMUNITY EDITION, electronic data capture system, source documentation and other relevant records for all enrolled subjects at the site. It is important that the Investigator and other relevant site personnel are available for consultation with the study monitors during the monitoring visits and that sufficient time is devoted at the site to the monitoring process.

If a deficiency is noted during an on-site visit (or at any other time during the course of the registry), the study monitor is required to discuss the situation with the Investigator and the Sponsor (if required) to secure compliance.

10.0 SPONSOR RESPONSIBILITIES AND RECORDS

10.1 Modification of Protocol

Any amendment to this protocol must be signed and dated by the Sponsor and the Investigator prior to its implementation. In the event the modification has the potential to impact the scientific soundness of the investigational plan or the rights, safety, or welfare of the human subjects involved in the investigation, the modification also will require IRB approval prior to its implementation. Any changes to the investigational plan that affects the rights, safety and welfare of the human subjects will most likely require a modification of the informed consent. Any changes to the informed consent will also require IRB approval prior to implementation, and may require subjects already enrolled in the registry to sign a new informed consent.

10.2 Premature Termination of Registry

The registry may be terminated at any time in the event of the occurrence of serious or unexpected adverse events that are determined by the Sponsor or the Investigator to pose a significant safety concern. In addition, the registry may be terminated at any time in the event of the occurrence of information that indicates that the device will not be commercially viable, or in the event that the Sponsor can no longer fund the registry.

The Sponsor will notify the Investigator in the event of premature termination of the registry. Further registry enrollment will be terminated at that time. Follow-up visits will continue for all enrolled subjects to ensure their safety. All subjects experiencing adverse events will be followed to resolution or until they are considered to be medically stable by the Investigator.

10.3 Serious Adverse Event Reporting

All carotid procedure and device related serious adverse events that are associated with the use of the device will be evaluated in accordance with the protocol and the Sponsor's Incident/Event Reporting SOP. Any serious adverse event that requires a Medical Device Report will be reported by the Sponsor to FDA in accordance with the Sponsor's Medical Device Reporting SOP.

10.4 Sponsor Records

The Sponsor shall maintain complete, accurate and current records for the registry, including the following materials:

- Copies of the approved registry protocol and any revisions;
- All correspondence with the Investigator and site personnel, and the IRB;
- Site information including address and IRB information;
- Investigators' curriculum vitae;
- Registry records including copies of IRB submissions and approvals for the registry, IRB approved consent forms and any modifications (and associated approvals);
- Receipt and maintenance of all data as collected on CRFs in SUGAR COMMUNITY EDITION, electronic data capture system.for the registry;
- Reports of device malfunctions and failures; and
- Reports of carotid procedure or device related adverse events, including SAEs, DRSAEs and UADEs.

11.0 DATA MANAGEMENT/DATA ANALYSIS/FINAL REPORT

11.1 DATA MANAGEMENT

The Investigator is responsible for the accurate completion and timely submission of the data collected during this registry. All data from this registry will be entered in SUGAR COMMUNITY EDITION, electronic data capture system. Data will be frequently reviewed to identify inconsistent or missing data and any carotid related adverse events. Any data issues are to be promptly addressed with the Investigator by the Sponsor or designated representative. Clinical procedures will be established to ensure that complete, accurate and timely data are submitted, that protocol requirements are followed and that carotid procedure or device related serious adverse events are correctly reported and investigated, as appropriate. The Investigator is to maintain all source documents as required by the protocol, including laboratory results, supporting medical records, and signed Informed Consent forms.

11.2 DATA ANALYSIS

For continuous variables such as subject age, the mean, standard deviation, median and range will be presented. For categorical variables such as presence of conditions observed under medical history, the number experiencing the condition over the total number completing the registry, the percentage, and the exact 95% confidence interval on the percentage will be presented.

Carotid procedure and device related serious adverse events will be listed and the time course, outcome, severity and possible relationship to the device will be documented.

Time to event analysis, when deemed necessary, will be performed using Kaplan Meier methods with any comparisons done via log-rank testing.

11.3 FINAL REPORT

A final report will be prepared by the Sponsor at the conclusion of this registry which will summarize all of the data collected, the parameters of all treatments and all carotid procedure and device related serious adverse events recorded during the registry. Copies of the final report will be provided to the Investigator and IRB.