PERFORM STUDY

A POST MARKET OBSERVATIONAL STUDY ON THE USE OF CORMATRIX® ECM® FOR FEMORAL ARTERIAL RECONSTRUCTION

STUDY SPONSOR:
CORMATRIX CARDIOVASCULAR, INC.
1100 OLD ELLIS ROAD
ROSWELL, GA 30076

PROTOCOL NUMBER: 14-PR-1120
REVISION: C

January 11, 2016

Please Note: Confidential information contained herein is made available to you in your capacity as Investigator, Medical Advisor, or Consultant to CorMatrix Cardiovascular, Inc. ("CorMatrix"). It is provided only for review by you, your staff, IRB/Ethics Committee members, or other regulatory authority. Except as necessary to obtain properly informed consent for participation, it is expected that there will be no disclosure to other persons.

Investigator Statement of Compliance

I hereby agree to comply with this protocol and applicable regulations governing clinical trials, including local regulations, and Good Clinical Practice / ICH Guidelines.

Investigator Signature: _____

Date: _____

Table of Contents –

CorMatrix Cardiovascular, Inc.

STUDY COORDINATION

STUDY SPONSOR	**CORMATRIX CARDIOVASCULAR, INC.** 1100 OLD ELLIS ROAD ROSWELL, GA 30076
DATA COORDINATION CENTER	**CORMATRIX CARDIOVASCULAR, INC.** 1100 OLD ELLIS ROAD ROSWELL, GA 30076

Study Synopsis

OBJECTIVE	The objective of the study is to actively gather additional information on the use of CorMatrix ECM for vascular repair in the reconstruction of the femoral artery.
STUDY POPULATION	Up to 5 clinical sites will enroll up to 100 subjects who have received CorMatrix ECM for vascular repair.
INDICATIONS FOR USE	The CorMatrix® ECM® for Vascular Repair is intended for use as a patch material for repair and reconstruction of peripheral vasculature including the carotid, renal, iliac, femoral, and tibial blood vessels. The CorMatrix ECM for Vascular Repair may be used for patch closure of vessels, as a pledget, or for suture line buttressing when repairing peripheral vessels.
ENDPOINTS	The endpoint is defined as the proportion of subjects with device related adverse events.
EXAMINATION SCHEDULE	The examination schedule is as follows: Pretreatment/treatment, four to six weeks, six months and twelve months following femoral arterial reconstruction with the CorMatrix ECM for vascular repair.
CLINICAL PARAMETERS	The following clinical assessments will be performed: • Assess medical history at baseline • Assess medications at baseline and for changes at all follow up visits • Device related adverse event assessment at treatment, 4-6 weeks, 6 months and 12 months • Duplex imaging at 4-6 weeks, 6 months and 12 months

1. Introduction and Rationale

Atherosclerosis and thrombosis are the main pathological processes involved in ischemic stroke, coronary heart disease and peripheral arterial disease. The disease prevalence of systemic atherosclerosis is approximately 3% to 10%, increasing to 20% in persons aged 70 years and older. Femoral endarterectomy with patch angioplasty has been the favored approach to the treatment of patients with symptomatic common femoral artery (CFA) occlusive disease. Primary patency rates of 74% to 91% at 5 years have been reported in the literature.

The development of carotid patches, as well as patches for use in arteriotomy closure elsewhere, continues to remain a critical adjunct for vascular surgery. The CorMatrix ECM for vascular repair is an attractive vascular patch material due to its ability to be remodeled into healthy native tissue.

The CorMatrix ECM for Vascular Repair acts as a decellularized scaffold for use as a vascular patch to repair the peripheral vessels. The extracellular matrix (ECM) scaffold is a biomaterial derived from porcine small intestinal submucosa (SIS). The SIS is developed from a select layer of tissue that is recovered from porcine small intestine. The decellularized ECM scaffold allows the patient's own cells to migrate and attach within the ECM to naturally repair the tissue defect.

CorMatrix Cardiovascular, Inc. received FDA 510(k) premarket clearance for the CorMatrix ECM for Vascular Repair on July 16, 2014. This Phase IV, post market observational study, will evaluate the safety and effectiveness of CorMatrix ECM for femoral arterial reconstruction by collecting specific data at pretreatment, treatment, 4-6 weeks, 6 months and 12 months following femoral arterial reconstruction with the CorMatrix ECM for vascular repair. Data collected from this study will not be used to support a marketing claim or change in labeling. This study is being performed to gather post-market data only and is not being performed under the direction of the FDA.

2. Indication for Use

The CorMatrix® ECM® for Vascular Repair is intended for use as a patch material for repair and reconstruction of peripheral vasculature including the carotid, renal, iliac, femoral, and tibial blood vessels. The CorMatrix ECM for Vascular Repair may be used for patch closure of vessels, as a pledget, or for suture line buttressing when repairing peripheral vessels. The entire Instructions for Use can be found in Appendix C.

3. Description

The CorMatrix® ECM® for Vascular Repair is intended for use as a patch material for repair and reconstruction of peripheral vasculature including the carotid, renal, iliac, femoral, and

tibial blood vessels. The CorMatrix ECM for Vascular Repair may be used for patch closure of vessels, as a pledget, or for suture line buttressing when repairing peripheral vessels.

The CorMatrix ECM for Vascular Repair is an extracellular matrix (ECM) scaffold derived from porcine small intestinal submucosa (SIS). The device is constructed of a multilaminate (6-ply), decellularized, non-crosslinked, lyophilized ECM cut to specific shapes and sizes and terminally sterilized using Ethylene Oxide gas. The CorMatrix ECM for Vascular Repair will be supplied as a 6-ply, lyophilized, sterilized sheet of SIS-ECM.

4. Prior Clinical Evaluations

CorMatrix ECM has been studied in previous prospective clinical evaluation, and a post-market clinical study is ongoing. The ECM for Pericardial closure has been studied in a randomized, prospective study to evaluate its ability to reduce the incidence of new onset atrial fibrillation; the ECM for Carotid Repair is under evaluation in a post-market study to capture and assess device performance data from subjects undergoing patch angioplasty of the carotid artery following carotid endarterectomy using the product per its FDA-cleared Indications for Use.

4.1 Post-market Clinical Evaluation of the ECM for Carotid Repair

CorMatrix is currently conducting a post-market registry study for the CorMatrix ECM for Carotid Repair (Protocol No. 11-PR-1021). 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 commercial 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. 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.

One-hundred and eighty six patients are enrolled in the study and included in the interim analysis of the CorMatrix ECM for Carotid Repair registry. The data demonstrated that the rate of device related adverse events were consistent with the rates found in the review of the contemporary literature for patch angioplasty. Specifically, no unanticipated events were found and the rate of the events was as anticipated in the risk management plan. Of specific interest in the analysis was the rate of pseudoaneurysm, which was present in 2 (1.08%) of the 186 patients and compared favorably to the rates found in the literature (1.4% to 5%).

The mean carotid stenosis (maximum) at pre-operative was 85.5%. Mean change from baseline values were -52.5%, -53.9%, -58.4%, and -45.2% at the 1- to 3-month, 6-month, 12-month, and 24-month follow-up evaluations. The mean carotid stenosis (minimum) at pre-operative was 72.5%. Mean change from baseline values were -64.5%, -63.7%, -

63.2%, and -60.4% at the 1- to 3-month, 6-month, 12-month, and 24-month follow-up evaluations.

As a result of this analysis and the directed and ongoing risk management activities, the overall residual risk of the CorMatrix ECM for Carotid Repair is determined to be acceptable.

5. Study Objectives

The objective of the study is to actively gather additional information on the use of CorMatrix ECM for vascular repair in the reconstruction of the femoral artery.

Endpoint
The endpoint is defined as the proportion of subjects with device related adverse events.

6. Study Design

This is a multi-center, Phase IV, prospective, single arm, post-market observational study of subjects undergoing femoral arterial reconstruction using the CorMatrix ECM for vascular repair per its FDA cleared Indications for Use. It is anticipated that up to 5 eligible sites will participate enrolling up to 100 subjects. Eligible candidates will be approached to ascertain interest in study participation. The approved Informed Consent and/or Patient Information Sheet will be completed and the process will be documented in the subject study binder by the research staff. Patients who have undergone a femoral arterial reconstruction using the CorMatrix ECM will be followed as per their usual standard of care. Information will be collected at follow up visits 4-6 weeks, 6 months and 12 months.

7. Study Population

Subjects are considered to be enrolled into this study at the completion of their surgical procedure of femoral arterial reconstruction with the use of CorMatrix ECM. Before any subject can be enrolled, the IRB for the specific institution must approve the protocol and the Informed Consent/Patient Information Sheet.

Subjects must meet the following requirements to be eligible for enrollment in this study:

Inclusion Criteria:

- Subjects must be undergoing femoral arterial reconstruction with patch angioplasty closure.
- Subject's surgeon intends to use CorMatrix ECM as the patch material for femoral arterial reconstruction per its FDA cleared Indications for Use.
- The subject must possess the ability to provide informed consent.
- The subject must express an understanding and willingness to fulfill all of the expected requirements of this protocol.

Exclusion Criteria:

- Known sensitivities to porcine material

8. Study Procedures

Study procedures are standardized to the extent possible and explained in detail below and are summarized in Table I - Study Procedure Overview.

All study-related data will be captured on standardized Case Report Forms. A copy of the Case Report Forms is provided in Appendix B. Case report forms will be sent to CorMatrix via fax at 678-990-2337 (attention S. Beall) or via scan/email to sbeall@cormatrix.com

Table 1: Study Procedure Overview

Activity	Pre-Tx	Treatment	Week 4-6	Month 6	Month 12
Assess Eligibility	X				
Informed Consent Process	X				
Medical History/update	X	X	X	X	X
Medication history/update	X	X	X	X	X
Duplex Imaging	X*		X	X	X
Surgical Complications		X			
Assessment for Adverse Events		X	X	X	X
Infection Information		X	X	X	X

*Data captured if performed, not required

8.1 Pre-Treatment Procedure

Patients presenting for femoral arterial reconstruction with patch angioplasty will be screened for study eligibility. Eligible candidates will be approached to ascertain interest in study participation. Before any study specific tests are performed, the patient will have the details of the study fully explained and will sign an approved Informed Consent or, if Waiver of Documentation of Consent, patient will verbalize understanding. The consent process will be documented by research personnel and the patient will be provided with a copy of the Informed Consent and/or Patient Information Sheet.

A pretreatment visit will be conducted prior to surgery and for all subjects:

- Documentation of the consent process
- Demographic information
- Medical history, including indication for surgery
- Duplex Imaging, if performed
- Relevant medications

8.2 Treatment Procedure

The subject will undergo a standard femoral arterial interventional procedure. The subject's femoral arteriotomy will be closed using the CorMatrix ECM for arterial repair. The Investigator will implant the CorMatrix ECM according to the FDA cleared Instruction for Use and per the surgeon's standard of care. Specific data on the procedure as well as the CorMatrix ECM will be collected. Device related adverse events will be documented on the case report form.

8.3 Post-operative

The Investigator's standard post-operative procedures will be followed. Post-operative data from the end of the procedure until the subject is discharged from the hospital will be collected and includes length of hospital stay, medications upon discharge and any complications/adverse events.

8.4 Follow up

Follow up assessments will be conducted at the 4-6 Week, 6 Month and 12 Month follow up visit per Table I - Study Procedure Overview. Data will be collected on the appropriate case report form.

9. Adverse Event Reporting

9.1 Definitions

Adverse Event (AE)
An adverse event (AE) will be defined as any undesirable clinical occurrence in a subject whether it is considered to be device related or not, that includes a clinical sign, symptom, or condition/observation of an unintended technical performance or performance outcome of the device. Causality is defined as not-related, possibly-related and probably-related to the device, which is further defined in Table 2: Event Relationship Assessment.

Serious Adverse Event (SAE)
A serious adverse event ("SAE") will be defined as an event that: 1) threatens life, 2) results in permanent impairment of a body function or permanent damage to a body structure, 3) necessitates medical or surgical intervention to preclude such impairment, 4) requires or prolongs hospitalization, or 5) is fatal (death).

Adverse Device Event
An Adverse Device Event will be defined as a clinical sign, symptom, or condition that is causally related to the device procedure, the presence of the device, or the performance of the device. Due to the temporal proximity of the AE to product administration, there is a

reasonable possibility that the product may have caused the AE or may have contributed to the severity or duration of an event caused by other means.

Table 2: Event Relationship

AE Relationship	Description
Not-related	A temporal relationship to the use of the product, which makes a causal relationship clearly and incontrovertibly due to extraneous causes, such as other drugs, products, chemicals, underlying diseases, environment, etc. Not-related to the use of the product.
Possibly-related	Occurring within a reasonable period of time relative to the use of the product, which makes a causal relationship possible, but plausible explanations may also be provided by other causes, such as other drugs, products, chemicals, underlying disease, environment, etc. Possibly-related to the use of the product.
Probably-related	Occurring within a reasonable period of time relative to use of product, which makes a causal relationship probable where the relationship cannot be attributed to other causes, such as drugs, products, chemicals, underlying disease, environment, etc. Probably-related to the use of the product.

9.2 Assessing and Recording Adverse Events

Each AE recorded must be documented on the Case Report Form. All serious and device related events must be reported immediately to CorMatrix via telephone or email within 24 hours of the Investigator becoming aware of the event. The case report form will be submitted to CorMatrix. The site will be contacted by CorMatrix for additional information including, but not limited to:

- Description of the event and underlying cause (diagnosis), coexisting disease, or other. In order to avoid vague, ambiguous, or colloquial expressions, the AE should be recorded in standard medical terminology rather than the subject's own words when possible.
- Date of onset and date of resolution. If the event is present at the Month 12 follow-up visit it will be marked as not resolved at study exit.
- Intensity of the event: mild, moderate, or severe.
- Frequency of the event: single episode, intermittent, or continuous.
- Action taken: none, medication, procedure, medication and procedure, or other.
- Relationship to the study treatment: not-related, possibly-related, or probably-related.

Any subject withdrawn from the study due to an AE will be followed until the outcome of the event is determined. The Investigator must ensure that the details of the event are documented in the medical notes including full details of the outcome, in addition to recording the event on the appropriate case report form.

All femoral 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 the FDA in accordance with Sponsor's Medical Device Reporting SOP. The site should contact:

Stephanie Beall
Project Administrator, CorMatrix
(470) 514-4031 (direct)
(678) 566-2628 (company)
sbeall@cormatrix.com

9.3 Possible Adverse Events

The following possible adverse events have been identified as possible risks from the CorMatrix ECM:

- 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 (superficial or deep)
- Patch dehiscence
- Pseudoaneurysm
- Recurrent stenosis
- Stroke
- Thrombosis
- Vessel occlusion

The following possible adverse events have been identified as possible risks from the surgical procedure:

- Reactions to anesthesia
- Bleeding
- Infection
- Nerve damage (skin numbness)
- Blood clots
- Hematoma
- Leg swelling
- Re-stenosis

This study will capture events reported at treatment, post-operatively, 4-6 Weeks, 6 months and 12 months follow up and as reported by the PI and/or subject and from a review of medical records.

10. Data Analysis

Since this is a Phase IV, post-market study, analyses will consist of tabulated data and descriptive statistics. Subject data listings and tabular and graphical presentations of the summary and statistical results will be provided. At a minimum, an interim report will be completed after 50 subjects have completed their four to six week follow-up. A final report will be completed at the end of the study. Additional quantitative and qualitative comparisons will be made to contemporary literature and similar studies.

11. Ethical Considerations

11.1 Code of Conduct

The Investigator will ensure that the clinical study is conducted in accordance with good clinical practice and all regulatory and institutional requirements, including those for subject privacy, Institutional Review Board or Ethics Committee approval, and record retention. (Appendix E: Investigator Qualifications and Responsibilities)

11.2 Ethics Committee / Institutional Review Board Approval and Oversight

The Investigator must obtain appropriate Ethics Committee ("EC") or Institutional Review Board ("IRB") approval before the study can be initiated. A copy of the written approval from the EC/IRB and a copy of the Informed Consent/Patient Information Sheet should be sent to CorMatrix. Appropriate study progress reports will be prepared for the EC/IRB by the Principal Investigator. Any changes to the protocol must be discussed and approved by CorMatrix in writing unless the change is made to assure the safety of the subject. In the non-emergent setting, after agreement on the changes has been reached, an amendment to the protocol will be provided by CorMatrix for submission to the EC/IRB for review and approval prior to initiation of the change. Any change made emergently must be documented in the subject's medical record. The Investigator must immediately forward to the EC/IRB any written safety reports or updates from CorMatrix.

11.3 Informed Consent Process and Subject Confidentiality

The investigator will be responsible for submitting the clinical study protocol and an Informed Consent or Patient Information Sheet (Waiver of Documentation of the Informed Consent Process) to their EC/IRB or centralized EC/IRB. The protocol, Informed Consent/Patient Information Sheet and the waiver must be approved by the local/centralized EC/IRB before the study is initiated and subjects enrolled.

Prior to obtaining any study specific information the approved Informed Consent must be signed and/or the Patient Information Sheet must be reviewed with the subject and the subject must provide verbal approval. Documentation of the consent process must be completed by the research personnel. The investigator shall provide a copy of the Informed Consent/Patient Information Sheet to the subject. Completed documentation of

the consent process will be available for auditing by CorMatrix or their representative, as applicable.

According to 45 CFR 46.117(c)(2) and 21 CFR 56.109 (c)(1), an IRB may waive the requirement for the investigator to obtain a signed consent form if:

a) The research presents no more than minimal risk of harm to participants and
b) The research involves no procedures for which written consent is normally required outside of the research context.

CorMatrix will maintain the confidentiality of the identity of subjects enrolled in the study and the information contained in their study records. CorMatrix will also instruct the study investigators in the importance of maintaining the confidentiality of study records. Any publication of any data collected as part of this trial will only use de-identified data, so that identification of any individual subject will not be possible. The records will be made available as required for review by the FDA, or other applicable regulatory agency and a reviewing EC/IRB; however to the extent possible, the subject's identity will not be disclosed. The Case Report Forms will use a subject identification number, with the patient name and address NOT appearing anywhere on the study form to be submitted to the sponsor (Appendix D: Sponsor's Commitments).

11.4. Clinical Study Monitoring

Study monitors qualified by training and experience will be responsible for monitoring and overseeing the conduct of this study. The Investigator shall cooperate with the study monitor designated by CorMatrix. This includes, but is not limited to, allowing the inspection of facilities utilized by the investigator for this clinical investigation, providing access to subject medical records for auditing and verification purposes, providing all required reports, and providing all other reports, including any subject report forms reasonably requested. The investigator, at reasonable times, shall also permit an authorized officer or employee of applicable regulatory agencies to inspect the facilities utilized by the investigator for the clinical investigation. The investigator will also permit this representative to inspect, copy, and verify records required as part of or relevant to the investigation.

Phone contacts and site visits will be conducted to ensure the protocol is being followed and all regulatory requirements are complete. Subject data will be reviewed and/or audited and all deficiencies corrected on site, if possible. A complete report will be made of all monitoring visits. When the study is terminated, a monitor will visit the site to ensure that all records are provided.

The monitor will review the study conduct to determine compliance with the study protocol Good Clinical Practice guidelines.

12. Bibliography

Sundermann SH, Rodriguez Cetina Biefer H, Emmert MY, Falk V. Use of Extracellular Matrix Materials in Patients with Endocarditis. *Thorac Cardiovasc Surg.* 2014; 62(1):76-79.

Toyoda Y, Kashem MA, Hisamoto K, Shiose A Tricuspid valve reconstruction with the extracellular matrix tube technique: A word of caution. *J Thorac Cardiovasc Surg*. 2014; Epub ahead of print.

Deorsola L, Pace Napoleone C, Abbruzzese PA Repair of an unusual aortic coarctation using an extracellular matrix patch. *Ann Thorac Surg.* 2014; 97(3):1059-1061.

Szczeklik M, Gupta P, Amersey R, Lall KS Reconstruction of the Right Atrium and Superior Vena Cava with Extracellular Matrix *J Card Surg*. 2014

Zaidi AH, Nathan M, Emani S, Baird C, Del Nido PJ, Gauvreau K, Harris M, Sanders SP, Padera RF Preliminary experience with porcine intestinal submucosa (CorMatrix) for valve reconstruction in congenital heart disease: Histologic evaluation of explanted valves *J Thorac Cardiovasc Surg*. 2014;Epub ahead of print.

Yanagawa B, Rao V, Yau TM, Cusimano RJ Potential myocardial regeneration with CorMatrix ECM: A case report. *J Thorac Cardiovasc Surg*. 2014; Epub Ahead of Print.

Wallen J, Rao V Extensive Tricuspid Valve Repair After Endocarditis Using CorMatrix Extracellular Matrix *Ann Thorac Surg*. 2014;97(3):1048-1050.

Cua CL, Kollins K, McConnell PI Echocardiographic Analysis of an Extracellular Matrix Tricuspid Valve. *Echocardiography*. 2014

Slachman FN Constructive Remodeling of CorMatrix Extracellular Matrix After Aortic Root Repair in a 90-Year-Old Woman *Ann Thorac Surg*. 2014; 97(5):e129-e131.

Witt RG, Raff G, Van Gundy J, Rodgers-Ohlau M, Si MS Short-term experience of porcine small intestinal submucosa patches in paediatric cardiovascular surgery. *Eur J Cardiothorac Surg*. 2013; 44(1):72-76.

Eckhauser AW, Hannon D, Molitor M, Scaife E, Gruber PJ Repair of Traumatic Aortoinnominate Disruption Using CorMatrix. *Ann Thorac Surg*. 2013; 95(4):e99-e101.

Wyler von Ballmoos M, Murtaza G, Gasparri M, Masroor S. Reconstruction of the right atrium using an extracellular matrix patch in a patient with severe mediastinal aspergillosis. *Int J Surg Case Rep.* 2013; 4(3): 290-292.

Yeen WC, Faber C, Caldeira C, Nallamshetty L, Haddad T, Rolfe M Reconstruction of pulmonary venous conduit with CorMatrix in lung transplant. *Asian Cardiovasc Thorac Ann*. 2013;21(3):360-362.

Yanagawa B, Rao V, Yau TM, Cusimano RJ Initial Experience With Intraventricular Repair Using CorMatrix Extracellular Matrix. *Innovations (Phila)*. 2013; 8(5):348-352.

Stelly M, Stelly TC. Histology of CorMatrix Bioscaffold 5 Years After Pericardial Closure. *Ann Thorac Surg.*2013; 96(5):e127-e129.

Weber SS, Annenberg AJ, Wright CB, Braverman TS, Mesh CL. Early pseudoaneurysm degeneration in biologic extracellular matrix patch for carotid repair. *J Vasc Surg.* 2013; Epub ahead of print Gerdisch MW, Shea RJ, Barron MD

Gerdisch MW, Shea RJ, Barron MD Clinical experience with CorMatrix ECM in the surgical treatment of mitral valve disease*J Thorac Cardiovasc Surg*. 2013;Epub ahead of print.

Kalangos A, Myers PO Aortic cusp extension for surgical correction of rheumatic aortic valve insufficiency in children. *World J Pediatr Congenit Heart Surg*. 2013; 4(4):385-391.

Slachman FN. Constructive Remodeling of CorMatrix ECM Following Aortic Root Repair in a 90 Year-old Female.*Ann Thorac Surg.* 2013.

Dearani JA, Said SM, O'Leary PW, Burkhart HM, Barnes RD, Cetta F. Anatomic repair of Ebstein's malformation: lessons learned with cone reconstruction. *Ann Thorac Surg.* 2013; 95(1):220-6; discussion 226.

Poulin F, Horlick EM, David T, Woo A, Thavendiranathan P. 3-Dimensional transesophageal echocardiography-guided closure of a Gerbode shunt due to CorMatrix patch dehiscence. *J Am Coll Cardiol.* 2013; 62(3):e5.

Quarti A, Nardone S, Colaneri M, Santoro G, Pozzi M. Valve leaflet reconstruction in pediatrics with extracellular matrix patch. *J Heart Valve Dis.* 2012; 21(1):138-139.

Sundermann SH, Biefer HR, Emmert MY, Falk V. Use of Extracellular Matrix Materials in Patients with Endocarditis.*Thorac Cardiovasc Surg.* 2012;Epub ahead of print. DOI: 10.1055/s-0032-1328920

Smith CR, Stamou SC, Boeve TJ, Hooker RC. Repair of a penetrating ascending aortic ulcer with localized resection and extracellular matrix patch aortoplasty. *Ann Thorac Surg.* 2012; 94(3):988-989.

Chalajour F, Barboza LA, Boni L et al. Reconstruction of pulmonary artery in a newborn using a porcine small intestinal submucosal patch. *Ann Thorac Surg.* 2012; 93(4):1311-1315.

Mavroudis CD, Casillan A, Rabbat M et al. Primary Intimal Sarcoma of the Pulmonary Vein with Extension into the Left Atrium: A Case Report. *Open Journal of Thoracic Surgery.* 2012; 2(2):25-28.

Tweddell JS, Mitchell ME, Woods RK, Spray TL, Quintessenza JA. Construction of the Right Ventricle-to-Pulmonary Artery Conduit in the Norwood: The "Dunk" Technique. *Operative Techniques in Thoracic and Cardiovascular Surgery.* 2012; 17(2):81-98.

Boyd WD, Tyberg JV, Cox JL. A review of the current status of pericardial closure following cardiac surgery. *Expert Rev Cardiovasc Ther.* 2012; 10(9):1109-1118.

Quarti A, Nardone S, Colaneri M, Santoro G, Pozzi M. Preliminary experience in the use of an extracellular matrix to repair congenital heart diseases. *Interact Cardiovasc Thorac Surg.* 2011; 13(6):569-572.

Gerdisch MW, Akinwande AO, Matheny RG. Use of a novel acellular xenograft as a patch for aortic annular enlargement during aortic valve replacement. *Innovations.* 2010; 5(1):60-62.

Scholl FG, Boucek MM, Chan KC, Valdes-Cruz L, Perryman R. Preliminary experience with cardiac reconstruction using decellularized porcine extracellular matrix scaffold: human applications in congenital heart disease. *World Journal for Pediatric and Congenital Heart Surgery.* 2010; 1(1):132-136.

Boyd WD, Johnson WE, Sultan PK, Deering TF, Matheny RG. Pericardial reconstruction using an extracellular matrix implant correlates with reduced risk of postoperative atrial fibrillation in coronary artery bypass surgery patients. *Heart Surg Forum.* 2010; 13(5):E311-E316.

Piterina AV, Cloonan AJ, Meaney CL et al. ECM-based materials in cardiovascular applications: Inherent healing potential and augmentation of native regenerative processes. *Int J Mol Sci.* 2009; 10(10):4375-4417.

Appendix A: Sample Informed Consent/Patient Information Sheet

(to be provided as separate documents)

Appendix B: Case Report Forms

(to be provided as a separate document)

Appendix C: Instructions for Use

ENGLISH

CORMATRIX®

CorMatrix® ECM®
For Vascular Repair
Instructions for Use

Manufacturer:
CorMatrix Cardiovascular, Inc.
1100 Old Ellis Road
Roswell, GA 30076 USA
Phone: 1-470-514-4080
Fax: 1-678-680-5486
www.cormatrix.com

20438-032514

ENGLISH

Indications For Use
The CorMatrix® ECM® for Vascular Repair is intended for use as a patch material for repair and reconstruction of peripheral vasculature including the carotid, renal, iliac, femoral, and tibial blood vessels. The CorMatrix ECM for Vascular Repair may be used for patch closure of vessels, as a pledget, or for suture line buttressing when repairing peripheral vessels.

CAUTION: Federal (U.S.) law restricts this device to sale by or on the order of a physician.

CONTENTS: One (1) Sterile CorMatrix ECM for Vascular Repair

Product Description
The CorMatrix ECM for Vascular Repair acts as a decellularized scaffold for use as a vascular patch to repair the peripheral vessels. The extracellular matrix (ECM) scaffold is a biomaterial derived from porcine small intestinal submucosa (SIS). The SIS is developed from a select layer of tissue that is recovered from porcine small intestine. The decellularized ECM scaffold allows the patient's own cells to migrate and attach within the ECM to naturally repair the tissue defect.

How Supplied
The CorMatrix ECM is supplied STERILE. Provided that the integrity of the sterile pouch is not compromised in any way, it serves as an effective sterile barrier until the "Use By" (expiration) date printed on the pouch.

Contraindications
This CorMatrix ECM is derived from a porcine source and should not be used in patients with a known sensitivity to porcine material.

Warnings And Precautions
- For single patient use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization will compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death.
- Discard all open or unused portions of the CorMatrix ECM.
- Device is sterile if the package is dry, unopened and undamaged. Do not use if the package seal is broken.
- The device must be used prior to the expiration date.
- Discard device if mishandling has caused possible damage or contamination.
- Always handle the device using aseptic technique.
- Ensure that the device is hydrated prior to suturing. Without proper hydration, the ECM may tear and not retain sutures. Additionally, excessive hydration may result in delamination. If delamination is observed, do not use the CorMatrix ECM.
- Device is not recommended to be used with glue containing glutaraldehyde.
- Device must be sutured to viable native tissue and must not be sutured to synthetic or chemically cross-linked materials.
- Device is not recommended to be used with platelet gel.
- Device is not recommended to be used with resorbable suture material.
- Once hydrated, the CorMatrix ECM should either be used or discarded. The CorMatrix ECM should not be rehydrated.
- If surgical intervention such as vessel cannulation is required after implantation of CorMatrix ECM, caution should be exercised not to damage the implanted CorMatrix ECM.

Potential Complications
The following complications are possible. If any of these conditions occur, the CorMatrix ECM should be removed.
- 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

Storage
This device should be stored in a clean, dry location at 10° to 30° Celsius.

Sterilization
This device has been sterilized with ethylene oxide gas.

Required Materials
- A sterile dish (kidney dish or other bowl)
- Sterile forceps
- Hydration fluid: At least 50mL of room temperature sterile water, sterile saline or sterile lactated Ringer's solution

ENGLISH

Suggested Instructions For Using The CorMatrix ECM
These recommendations are designed to serve only as a general guideline. They are not intended to supersede institutional protocols or professional clinical judgment concerning patient care. The CorMatrix ECM for Vascular Repair is MR Safe in that it poses no known hazards in MR environments.

1. Using aseptic technique, remove the inner pouch from the outer pouch, and place the inner pouch containing the CorMatrix ECM into the sterile field.
2. Open the inner pouch carefully, and aseptically remove the CorMatrix ECM with sterile forceps.
3. Hydrate the CorMatrix ECM by placing it in a bowl of sterile saline or other sterile isotonic solution for approximately 1-2 minutes prior to use. Use at least 50mL of the sterile solution for hydration. It is recommended that the ECM not be excessively handled or manipulated prior to use.
4. Prepare the tissue deficiency/defect or treatment area using standard methods.
5. If required, the CorMatrix ECM can be cut to the appropriate size, using aseptic technique, in order to adequately cover the tissue deficiency/defect or treatment area. If delamination is observed, do not implant the CorMatrix ECM.
6. Place the edge of the CorMatrix ECM in contact with viable tissue. To ensure adequate remodeling, it is important that the CorMatrix ECM is sewn to viable tissue.
7. Suture the CorMatrix ECM to the area of treatment or tissue deficiency/defect. A non-absorbable monofilament suture is preferred.
8. Complete the standard surgical procedure.
9. Discard any unused portions of the CorMatrix ECM.

Return Goods Policy
For information on product returns and return authorization, contact CorMatrix Cardiovascular by calling 1-470-514-4080. All products returned to CorMatrix Cardiovascular must be accompanied by a Return Goods Authorization Number.

Medical Device Reporting
Any potential adverse incident involving CorMatrix Cardiovascular products should be reported immediately by calling 1-470-514-4080.

Warranty And Limitation Of Liability
CorMatrix Cardiovascular, Inc. warrants that the product when delivered is free from defect in materials and workmanship and conforms to the manufacturer's product specifications. This warranty applies for the period of time up to and including the expiration date of the product. At its option, CorMatrix Cardiovascular will replace or provide a refund for this product if it is found to be defective. The product must be returned to CorMatrix Cardiovascular in the original packaging with the lot number, or according to the return goods policy. CorMatrix Cardiovascular shall not be liable for any incidental or consequential loss, damage, or expense, directly or indirectly arising from the use of, or inability to use, its product.

THE FOREGOING WARRANTY IS IN LIEU OF AND EXCLUDES ALL OTHER WARRANTIES, WHETHER EXPRESSED OR IMPLIED, ARISING BY OPERATION OF LAW OR OTHERWISE, INCLUDING ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

CorMatrix Cardiovascular neither assumes, nor authorizes any person to assume for it, any other additional liability or responsibility with respect to this product other than as set forth in writing herein.

Symbols And Their Explanations

	Use By	STERILE EO	Sterilized using Ethylene Oxide
10° 30°	Store at 10° C - 30° C		Do Not Reuse
	Consult Instructions for Use		Do Not Resterilize
			Do Not Use if the Package is Damaged or Open
LOT	Lot Number		Non-pyrogenic
REF	Catalog Number		Manufacturer

Appendix D: Sponsor Commitments

CorMatrix is committed to:

1. Complying with the Declaration of Helsinki and all applicable health authority regulations governing the conduct of clinical research studies.
2. Protecting the rights, health, safety and welfare of study subjects.
3. Informing the clinical investigators of any new information about the study which may affect the health, safety, or welfare of the subjects, or may influence their decision to continue participation in the study.
4. Providing the clinical investigators with the study protocol and Case Report Forms on which to document the study evaluation variables for each subject entered into the study.
5. Providing the clinical investigators and study staff training on the protocol and completion of the Case Report Form.
6. Providing the statistical analysis and study report writing resources necessary to complete reporting of the study results.
7. Certifying that EC/IRB approval of the protocol and Investigators Agreement will be completed prior to treatment at a clinical site.

Appendix E: Investigator Qualifications and Responsibilities

Each investigator must be a licensed physician who has received training for using the CorMatrix ECM for Vascular Repair. The investigators have the following responsibilities:

1. Subject Selection

The investigator is responsible for assuring that all subjects entering the study are eligible to participate.

2. Ethics Committee (EC)/Institutional Review Board (IRB) Approval

The investigator must obtain approval for his participation in this protocol from an EC/IRB prior to entering any patients in the study. Assurance that the EC/IRB approval of the study protocol and Informed Consent and/or Waiver of Documentation of Consent has been obtained will be provided to the Sponsor prior to initiation of the study.

3. Subject Evaluation and Data Reporting

The investigator is responsible for performing the patient evaluations as described in the study protocol. All information generated by the patient evaluation will be recorded on the Subject Case Report Forms provided by the Sponsor. The Case Report Forms will be filled out in black ink. Any corrections will be made by lining out with a single line, providing the date of corrections and initials of person making the correction. Correction fluid will not be used. The Investigator will sign and date the forms and will send the form via fax / email to CorMatrix. Copies of all Case Report Forms will be retained in the Investigator's office in order to be available for monitoring by CorMatrix personnel or by authorized regulatory agencies.

Investigator(s) will not deviate from the protocol without prior approval of CorMatrix unless protection of the health, safety or welfare of study subjects requires prompt attention.

4. Record Retention

The Investigator must retain all subject records for at least 2 years, or longer, if required by local regulations.