Study Title: Post-market, prospective evaluation of PHOTO-oxidized decellularized bovine pericardium used as a patch in Vascular repair and reconstruction surgery: PHOTO-V

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Study Title:	Post-market, prospective evaluation of **PHOTO-**oxidized decellularized bovine pericardium used as a patch in **V**ascular repair and reconstruction surgery: ***PHOTO-V***
Study Article Name:	PhotoFix®

SPONSOR SIGNATURE PAGE

The signatures below constitute the approval of this protocol and the attachments.

Erin Hurley, Project Manager, Clinical Research — Date: 06/28/2018

Scott B. Capps, Vice President, Clinical Research — Date: 06/29/2018

William Northrup, M.D., Vice President Physician Relations and Education — Date: 06/29/2018

Virendra Patel, MD, MPH, Medical Expert — Date: 7/9/2018

CONFIDENTIALITY STATEMENT

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STATEMENT OF COMPLIANCE

This study will be carried out in accordance with Good Clinical Practice (GCP) as required by the U. S. Code of Federal Regulations applicable to clinical studies (45 CFR 46).

SIGNATURE PAGE

The signatures below constitute the approval of this protocol and the attachments, and provide the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local and legal and regulatory requirements and applicable US federal regulations and GCP guidelines.

Site Investigator:

Signed: _____ Date: _____

Name:

Title: Primary Investigator

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1 INTRODUCTION

1.1 Abbreviations

- **AAA**: abdominal aortic aneurysm
- **BMI**: body mass index
- **CAS**: carotid artery stenosis
- **CEA**: carotid endarterectomy
- **CTA**: computed tomography angiography
- **DSA**: digital subtraction angiography
- **eCRFs**: electronic case report forms
- **EDC**: electronic data capture
- **ESRD**: end stage renal disease
- **FDA**: food and drug administration
- **HAR**: hemodialysis access repair
- **IFU:** instructions for use
- **IRB:** institutional review board
- **MRA**: magnetic resonance angiography
- **PTFE:** polytetrafluoroethylene
- **PAD:** peripheral arterial disease
- **RRT**: renal replacement therapy
- **SDV**: source document verification
- **SOP**: standard operating procedure
- **TIA:** transient ischemic attack
- **UDI:** unique device identifier

1.2 Protocol Summary

The objective of this post-market clinical follow-up study is to evaluate safety endpoints in patients receiving PhotoFix® Decellularized Bovine Pericardium (PhotoFix) as a patch within a vascular repair or reconstruction procedure. PhotoFix is prepared from bovine pericardium, which is stabilized using a dye-mediated photo-oxidation process and sterilized using aseptic processing techniques. The primary endpoint for patients with carotid artery stenosis (CAS) undergoing carotid endarterectomies (CEA) will be rate of ipsilateral central neurologic events; the primary endpoint for all other vascular procedures will be primary patency. The secondary endpoints include all-cause reoperation rate, device-related reoperation rate, explant rate, restenosis rate, secondary patency (hemodialysis access repair (HAR) only) and survival. A goal of 100 patients will be enrolled at approximately 10 sites. The enrollment period will span a minimum of 8 months from Institutional Review Board (IRB) approval and site activation. Candidates for this study are adults who require vascular repair or reconstruction surgery that necessitates the use of a patch. Patients will be consented pre-operatively and enrolled patients will be followed for approximately 6 months after PhotoFix surgery. Data will be collected at 5 time points: baseline (pre-operatively), intra-operatively, 1 month post-operatively, 3 months post-operatively, and 6 months post-operatively. Patients will be required to return to the office for the 3 visits occurring after hospital discharge. Follow-up data collection will focus on the

safety endpoints; data will be abstracted from the patient's medical record and collected from patient self-report. Study specific testing, including imaging and laboratory testing, will not be required.

1.3 Study Title

Post-market, prospective evaluation of photo-oxidized decellularized bovine pericardium used as a patch in vascular repair and reconstruction surgery (PHOTO-V).

1.4 Study Objective

The objective of this post-market clinical follow-up study is to evaluate the clinical outcomes of patients receiving PhotoFix as a patch within a vascular repair or reconstruction procedure.

1.5 Clinical Background

Vascular disease is a prevalent medical issue, which can require affected patients to undergo surgery. The need for surgery is dependent on the indication, but can be required to reestablish blood flow, repair weakened artery walls, or create hemodialysis access. These surgeries can require the use of a vascular patch to close or repair defects; primary suture closure is not always an option.

Incidence Rates:
Vascular surgery is required for a variety of indications. A large percentage of vascular surgeries are performed due to CAS, peripheral artery disease (PAD), abdominal aortic aneurysm (AAA) and HAR in patients with end stage renal disease (ESRD). These combined conditions represent a large population of individuals. Not all patients require surgical intervention; however, many patients, including those who are asymptomatic, will undergo surgery to prevent potential long term complications.

The prevalence of CAS has been reported to affect 3.4% and 4.2% of females and males, respectively.[1] The prevalence of CAS varies by race, with increased risk in Caucasians and Native Americans.[1] The worldwide prevalence of PAD has been estimated at greater than 200 million people.[2] A recent meta-analysis estimated a pooled prevalence for AAA to be 4.8%, with obvious global variance, with higher prevalence in Australia compared to America and Europe.[3]

Lastly, the worldwide number of patients who received renal replacement therapy (RRT) was recently estimated as 2.6 million. A conservative estimate determined that the number who received RRT vastly underestimates the total who need it; an estimated 4.9 million people need RRT.[4] For those requiring hemodialysis, a type of RRT, arteriovenous fistula and arteriovenous graft are generally preferred over long-term central venous catheter. However, these options require surgical interventions to create and maintain access. In these cases, patches may be required to repair and reconstruct defects.

The intention of vascular patching is to improve blood flow, vessel geometry and biomechanics.

Alternative Treatments for Vascular Surgery Requiring Patch Material:
Currently available patch materials include vein patches (saphenous or neck veins) and synthetic patches (polytetrafluoroethylene (PTFE), Dacron, or bovine pericardium). Selection of the ideal patch material is a debated topic; anatomical characteristics, availability, comorbidities, and patch indication are considered within the selection process. The theoretical benefit of autologous patches include an increase in luminal size, provision of endothelialized tissue to the patch site, less thrombogenicity, and increased resistance to infection.[5] However, issues with availability, increased operative time, harvesting-related morbidity, and late aneurysmal dilatation have been reported with autologous patch use.[5] Synthetic patches have been used as an alternative; early criticisms of these patches included prolonged hemostasis time and increased thrombosis.[5]

Clinical Results in Alternative Treatments:
There are numerous studies reporting results of vascular patches for cases of CAS requiring CEA. These studies have compared outcomes between patches and direct suture, as well as outcomes between different patch materials.

A recent systematic review and meta-analysis compared CEA outcomes over multiple studies.[6] Results from 10 studies comparing primary closure to patch closure were included in one of the meta-analyses. Amongst the 10 studies, patches included saphenous vein patches (n=3), synthetic patches (n=3), and combined vein and synthetic (PTFE or Dacron) (n=4).[6] Procedures using patches significantly reduced the risk of perioperative stroke and long-term stroke (OR = 0.49, $p = 0.02$).[6] The use of patches also reduced the risks of perioperative arterial occlusion (OR = 0.18, $p < 0.0011$) and long-term recurrent stenosis (OR = 0.24, $p < 0.01$).[6] Aggregate results from 9 studies were also compared in a meta-analysis; studies reported the comparison of vein and PTFE patches. Perioperative and long term rates of stroke, ipsilateral stroke, combined stroke and death and mortality were not different between groups.[6] Aggregate results from 4 studies compared Dacron to other synthetic patches.[6] At 30 days, Dacron was associated with higher risk of perioperative stroke and transient ischemic attack (TIA) ($p=0.03$) and restenosis ($p=0.004$).[6] There was also significantly more strokes ($p=0.03$), combined stroke and death ($p=0.02$), and arterial restenosis ($p<0.001$) with Dacron during longer term follow-up.

Marien et al. compared peri and post-operative outcomes between CEA patients who received bovine pericardium (n=51) and Dacron (n=44).[7] Suture line bleeding at 3 minutes and 4 minutes was significantly higher in the Dacron group (55% vs. 14%, $p<0.001$, 30% vs. 4%, $p=0.001$ respectively).[7] The surgeons also reported that bovine pericardium had superior handling characteristics compared to Dacron.[7]

There is limited published data comparing vascular patch outcomes in surgeries for AAA, PAD or HAR. One small retrospective study compared patency outcomes in HAR with stenting (n=34) vs. patch angioplasty (n=15).[8] Initial post-interventional patency and patency after secondary reintervention were not statistically different between patients who received a patch and those who were stented; however, patch angioplasty trended towards reduced patency after second reintervention.[8]

PhotoFix Decellularized Bovine Pericardium:
There is still a need for vascular patches with mechanical properties that mimic natural tissue, resist deterioration and do not increase the risk for restenosis and other device-related complications. PhotoFix offers another option to vein patches and other synthetic patches, specifically, glutaraldehyde treated xenografts. PhotoFix tissue is treated through dye-mediated photo-oxidation; the processing stabilizes the internal collagen structure while eliminating toxic by-products which allow calcium to bind to the tissue. Dye-mediated photo-oxidation was first described in the medical literature in the 1990's.[9] The treated tissue was described as "stable toward chemical, enzymatic, and in vivo degradation while maintaining physical properties of natural tissue".[9] Moore expanded on the PhotoFix process in 2001 by further describing the material as "biostable, biocompatible, relatively nonclacific, and flexible".[10]

Biomechanical Testing Results:
PhotoFix mechanical testing has demonstrated that the patch is either superior or comparable to currently marketed patches in terms of tear resistance strength, ultimate tensile strength, suture retention, and ball burst strength. Testing was completed on CryoLife-manufactured product and evaluated the device's average force of failure. The average maximum load for suture retention, ultimate tensile strength, ball burst strength, and tear resistance were 8.39 N, 15.6 N, 309.85 N, and 7.3 N, respectively.

Biocompatibility Results:
Biocompatibility testing was performed under the guidance from ISO 10993-1. The specific biocompatibility testing performed for PhotoFix is consistent with the exposure duration of the product and its intended use (i.e. permanent exposure of product in contact with blood). The full battery of tests supports the biocompatibility of the device.

Preclinical Results:
PhotoFix (formerly CardioFix) was implanted in a rat subcutaneous study which concluded that the test article had excellent biostability (greater than 71%) and low to minimal calcification. PhotoFix was also examined in a 20-week sheep study. PhotoFix was implanted within the pericardial sac, in the atrial septal, and the ascending and descending aortic positions. There was no evidence of creep or stretching, structural degradation, or collagen degradation. There was also no evidence of thrombogenicity, infection, excessive inflammation or intrinsic calcification. Overall, the testing demonstrated acceptable *in vivo* performance in cardiovascular and pericardial repair applications. These results in a cardiac model can be considered applicable to its use in peripheral or non-cardiac vascular indications since cardiac conditions represent more exaggerated conditions of pressure, contractility and stretching.

The PhotoFix biocompatibility data, photo-fixation data, pre-clinical data, and clinical literature of equivalent devices support the safety of the device. Post-market clinical follow-up through a clinical study will support active surveillance efforts to identify any residual risk.

2 GENERAL INFORMATION

2.1 Device Generic Name
Decellularized Bovine Pericardium

2.2 Device Trade Name
PhotoFix®

2.3 Device Manufacturer
CryoLife®, Inc.
1655 Roberts Blvd., NW
Kennesaw, GA 30144

2.4 Study Sponsor Contact
Erin Hurley

1655 Roberts Blvd., NW
Kennesaw, GA 30144
Phone: 678-290-4627
Fax: 770-590-3749
Email: hurley.erin@cryolife.com

2.5 Device Description
PhotoFix is prepared from bovine pericardium, which is stabilized using a dye-mediated photo-oxidation process; it is processed using ethylene oxide and sterilized using aseptic processing techniques. No aldehyde chemistry is used during any phase of pericardium manufacturing, including the tissue fixation and sterilization processes. All available patch sizes, with respective product codes, are listed in Table 1.

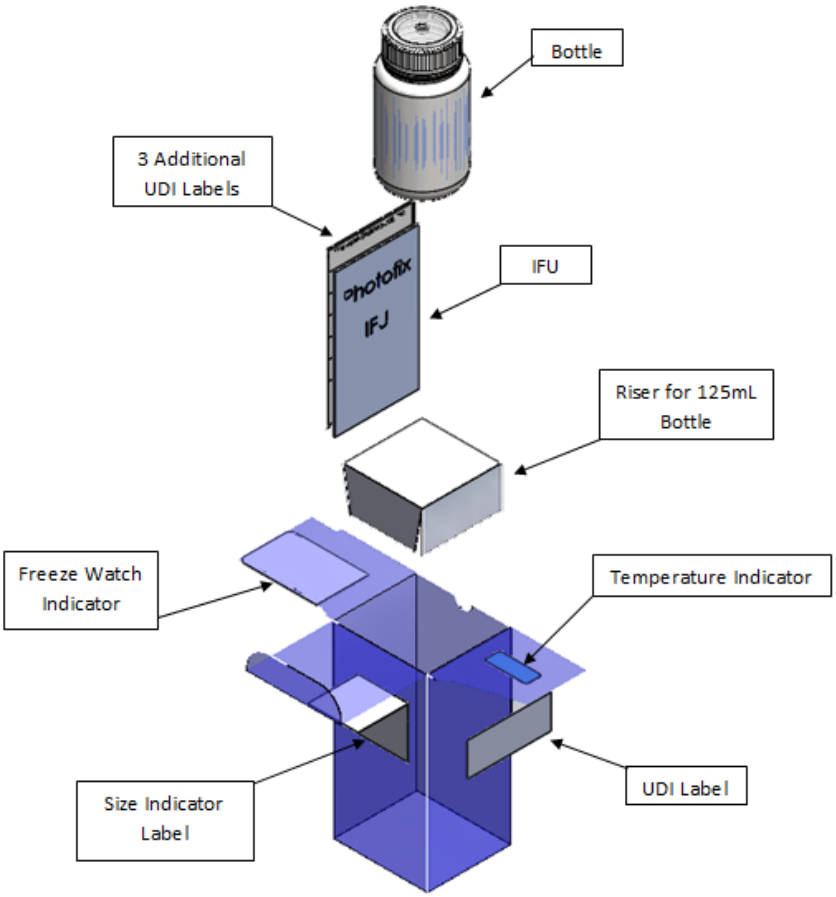
Table 1: PhotoFix Patch Sizes and Product Codes

Description/ Patch Size	Product Codes
PhotoFix 6cm x 8cm	PFP6X8 / PFP6X8-G
PhotoFix 0.8cm x 8cm	PFP0.8X8 / PFP0.8X8-G
PhotoFix 1cm x 6cm	PFP1X6 / PFP1X6-G
PhotoFix 4cm x 4cm	PFP4X4 / PFP4X4-G
PhotoFix 1cm x 10cm	PFP1X10
PhotoFix 2cm x 9cm	PFP2X9
PhotoFix 1cm x 14cm	PFP1X14

2.6 Identification of Critical Components
The PhotoFix primary packaging system consists of the container (Nalgene bottle), which stores the tissue in 22% buffered ethanol solution, and the closure (screw on cap using a torque limited closure device) which prevents leakage of the solution. A tamper evident shrink band is then applied around the bottle and the cap.

The PhotoFix secondary packaging consists of a PhotoFix shelf box, temperature indicator, and freeze-watch indicator. The secondary packaging also holds additional unique device identifier (UDI) labels and the Instructions for Use (IFU). Figure 1 illustrates the packaging configuration for PhotoFix.

Figure 1: PhotoFix Packaging Configuration



2.7 Materials Used

PhotoFix is manufactured from bovine pericardium derived from bovines born in Australia, New Zealand, or the United States.

2.8 Intended Use

PhotoFix is indicated for the following uses: vascular repair and reconstruction (for example: the carotid, iliac, femoral, and tibial blood vessels and arteriovenous access revisions).

2.9 Regulatory Status

United States:

PhotoFix is classified as Class II per 21 CFR 870.3470- Intracardiac patch or pledget made of polypropylene, polyethylene terephthalate, or polytetrafluoroethylene.

3 EXPERIMENTAL DESIGN

3.1 Type of Study

This study is a prospective, multicenter, post-market clinical follow-up study to evaluate PhotoFix safety outcomes in vascular repair and reconstruction surgery. This is an observational study on a currently marketed device; no study activities are experimental.

3.2 Study Size & Duration

Patients will be enrolled at approximately 10 sites. The enrollment period will span the time needed to consent approximately 166 patients. The target sample size is 100; projected enrollment considers a screen failure rate of 33% and an early termination rate of 10%. Enrollment is estimated to take a minimum of 8 months from Institutional Review Board (IRB) approval and site activation. Enrollment will begin at the principal investigator's site and in agreement with all central and local IRB requirements. The enrollment period will continue until the Sponsor decides to stop enrollment. The Sponsor will activate additional sites at their discretion.

A singular anatomical region will be selected for patch use. More than one patch can be used within the repair or reconstruction of this target region. However, patients requiring patches at distinct anatomical regions will be excluded. Additionally, patients undergoing concomitant procedures requiring additional prosthetics (e.g. stents) will be excluded. For complex cases, where clarification on these criteria is required, the Sponsor should be contacted prior to obtaining consent.

Patients undergoing a vascular procedure which falls within the indications for use and requires the use of PhotoFix will be screened and consented for the study, pre-operatively.

The study will collect prospective data at 5 time points; data will be collected pre-operatively, intraoperatively/immediately post-operatively, 1 month post-operatively, 3 months post-operatively, and 6 months post-operatively. All study patients will be expected to participate in all study required evaluations. Patients will be expected to come into the office at the 3 follow-up visits, post hospital discharge. For all post-operative visits outside the hospital, a +/- 14 day window is allowed for schedule fluctuations, but visits should ideally remain at the intended intervals. Data will also be collected on any unscheduled events (i.e. reoperation, explants, etc.) which may occur during the study period.

Patient demographics and medical history, including medications, comorbidities, pertinent surgical history, and fundamental vascular diagnosis, will be collected at time of consent. Medications will only include drugs of interest and will not require a complete listing. Adverse events will be collected after surgery on all patients consented and enrolled into the study. The investigation will be conducted for a period necessary to collect all follow-up, as needed on each patient, but will not exceed 7 months after surgery. The total time a patient will be followed will be determined by their date of surgery; dates of surgery should occur within 60 days of consent. If the patient's surgery is scheduled after 60 days, a re-screen request must be submitted to the Sponsor. The anticipated final follow-up will be conducted in November 2019, but will ultimately be determined by IRB approvals, site activation, and by rate of patient enrollment.

3.3 Study Population

Candidates for this study are adults who require vascular repair or reconstruction surgery that necessitates the use of a patch. Examples of vascular procedures include the repair and reconstruction of the carotid, iliac, femoral, and tibial blood vessels, as well as arteriovenous access procedures.

Study patients will be evaluated by medical history, disease process, and anatomic suitability for the study. To be enrolled in the study, candidates must meet the following Inclusion and Exclusion Criteria.

3.3.1 *Inclusion Criteria*:

- Patient is undergoing a vascular procedure which falls within the indications for use and requires the use of PhotoFix Decellularized Bovine Pericardium
- Patient's surgery is anticipated to occur within 60 days of consent
- Patient is ≥18 years old
- Patient is willing and able to comply with the protocol and follow up period
- Patient is willing and able to give written informed consent

3.3.2 *Exclusion Criteria*:

- Patient's procedure is a revision of a prior arteriotomy or venotomy
- Patient's procedure requires multiple vascular patches in anatomically distinct regions or other prosthetics (e.g. stents)
- Patient has a medical history of abnormal coagulopathy, bleeding, or thromboembolic disease
- Patient has a medical history of severe immunodeficiency disease
- Patient has a medical history of cancer
- Patient has severe visceral disease in heart or active liver disease or icterus
- Patient has a history of cerebrovascular accident (completed stroke) within 3 months of planned surgery
- Patient has a history of atrial fibrillation and requires a patch for carotid endarterectomy repair
- Patient has an active or potential infection at the surgical site
- Patient has used or plans to use immunomodulatory drugs for ≥ 6 months
- Patient has a sensitivity to products of bovine origin
- Patient is currently enrolled in another study
- Patient has a life expectancy of less than 12 months
- Patient is pregnant or breastfeeding or planning on becoming pregnant or unwilling to use medically acceptable methods of birth control
- Patient's procedure is emergent

3.4 Study Activities

Patients will be carefully evaluated before being consented into the study. Patients will be considered for screening after diagnostic evaluation has confirmed that the patient is a candidate

for vascular surgery and it is determined that the surgery will require the use of a patch. Diagnostic evaluation may include known patient history, presentation with symptomology associated with need for surgery, and imaging (Computed Tomography Angiography (CTA), Magnetic Resonance Angiography (MRA), Duplex imaging, Digital Subtraction Angiography (DSA), etc.).

Screening and follow-up assessments will be performed in accordance with the schedule provided in Table 2. These screening assessments will evaluate the patient's medical and surgical history for inclusion in the study. The follow-up assessments will evaluate post-operative outcomes.

3.4.1 Patient Enrollment

Patients who provide written informed consent and meet the eligibility requirements will be consented into the study. This is an open-label single arm study, so no randomization will be performed.

Table 2: Schedule of Activities

PROTOCOL ACTIVITIES	**#1**: Pre-Op	**#2**: Intra-Op/ Immediately Post-Op	**#3**: 1 month Post-Op[4]	**#4**: 3 months Post-Op[4]	**#5**: 6 months Post-Op[4]
Informed Consent	**X**				
Eligibility Evaluation	**X**				
Baseline Assessments[1]	**X**				
Imaging Evaluation[2]	**X**	**X**	**X**	**X**	**X**
Medication	**X**	**X**	**X**	**X**	**X**
Operative Assessment		**X**			
Adverse Event[3]		**X**			
Explant Evaluation[3]		**X**			
Follow-Up Evaluation			**X**	**X**	**X**
End of Study					**X**

[1]Includes the following: Demographics, Medical History, Surgical History, and Social History.
[2]If available, pre, peri, and post-operative imaging data (specific to the study) will be extracted from the patient's medical records by the site.
[3]Only reported if applicable and can happen at any point peri or post-operatively.
[4]Office visits windows are +/-14 days; however, visits should ideally remain at specified intervals.

3.4.2 Informed Consent

Prior to screening for the study, all patients will be informed in detail about the nature of the clinical study, as well as its risks, potential benefits and anticipated discomforts. All patients will also be informed about the use and disclosure of the patient's health information, referred to as "Protected Health Information (PHI)," for the clinical study. Patients will also be informed about their rights with respect to their PHI, and will be informed of the study site's legal duties under the Health Insurance Portability and Accountability Act (HIPAA, see Appendix A), and any local requirement.

The basic elements of HIPAA Authorization will be followed, as specified by 45 CFR 164.508, and any local requirement(s). HIPAA authorization will be incorporated into the Informed Consent Form (ICF).

The basic elements of informed consent will be followed, as specified by 21 CFR 50.25, and any local requirement(s). Written informed consent will be obtained from each patient to be involved in the clinical study using the IRB approved ICF. The primary investigator, or his/her designee, or a witness will verify consent as mandated by the site's IRB requirements.

All patients must provide written informed consent in accordance with the overseeing IRB regulations. The study site must use the ICF approved by the IRB and CryoLife. A sample ICF can be found in Appendix B.

3.4.3 Screening, Eligibility and Enrollment

All consented patients will be screened for potential inclusion in the study at a pre-operative visit. Any potential re-screens will need to be approved by CryoLife prior to reconsent. Patients will be assigned a unique, de-identified Screening ID. The ID will include a two-character site assigned ID, followed by a two-digit consecutive number. The Eligibility Evaluation will be used to assess eligibility at screening.

All data will be captured and entered into electronic case report forms (eCRFs). The following eCRFs will be completed at time of screening:

- Informed Consent
- Eligibility Evaluation
- Demographics
- Medical History
- Surgical History
- Social History
- Medication
- Imaging Evaluation (if applicable)

The patient will have undergone a comprehensive vascular assessment prior to screening, which may include diagnostic imaging and surgical consult. The Imaging Evaluation form will be used to capture all retrospective and prospective variables which are documented on available imaging reports, as it relates to the patient's PhotoFix surgery.

3.4.4 Surgical Procedures

All patients will undergo a vascular repair or reconstruction surgery, which requires the use of PhotoFix. The surgical procedures will vary by patient and by underlying etiology. Therefore, PhotoFix implant sites will also vary. In all cases, PhotoFix will be implanted per the Instructions for Use (IFU) (Appendix C).

Photographs may be taken perioperatively and will capture the patch site, before, during and after PhotoFix implant. A minimum of 3 photographs may be taken to include: the prepped target artery/vein, a point during the process of implanting PhotoFix, and after PhotoFix has been implanted (before surgical site closure).

3.4.5 Intraoperative Evaluation

Patients that meet the study criteria will receive PhotoFix as a vascular patch, per the IFU. A patient will remain eligible for continuation if PhotoFix remains implanted at the conclusion of their vascular surgery; patients would be considered enrolled at this point. Peri-operative and post-operative (<24 hours after surgery) data will be collected on all enrolled patients; this data will be entered into the Operative Assessment eCRF (Appendix D). The following measures will be monitored and documented per indication, but may include:

- Surgery date
- Implanting surgeon
- Number of PhotoFix Patches Used
- PhotoFix lot number(s)
- PhotoFix patch size(s) (indicated on box(es))
- Patch implant site
- Surgical procedure description
- Concomitant procedure description
- Any adverse events, device malfunctions, or intraoperative mortality
- Peri-operative imaging data

Any intraoperative adverse events will be captured on the Adverse Event eCRF (Appendix D). Patients will be told to contact the investigator in the event of any complications which occur during the study. The contact information for the Principle Investigator is included in the copy of the signed ICF each consented patient will have received.

3.4.6 Follow-up Visits

The patients will be asked to return for 3 post-operative visits at 1, 3, and 6 months after surgery. Available data from post-operative imaging reports will be collected, as is applicable to the study and entered into the Imaging Evaluation eCRF (Appendix D); the imaging is not a requirement of the study. Clinical data for all follow-up visits will be entered into the Follow-Up Evaluation eCRF (Appendix D). This form will collect data on post-operative recovery. The following measures will be monitored and documented per indication, but may include:

- Visit date
- Study status
- Loss of patency/ Evidence of restenosis
- Reoperations / vascular surgeries required post-op
- Any adverse events, explants, or other mortality
- Post-operative imaging data

4 ANTICIPATED COMPLICATIONS AND ADVERSE EVENTS

4.1 Anticipated Complications

For this study, a complication is defined as the following: morbid event or consequences of a morbid event. While all complications will be summarized in the final report, the primary focus of the analysis will be complications involving the vascular system, such as transient ischemic attack (TIA), amaurosis fugax, stroke, symptomatic carotid occlusion, thrombosis, bleeding, and death. The terms "adverse event" and "complication" will be used interchangeably.

An Adverse Event (AE), Unanticipated Adverse Effect (UAE) and Serious Adverse Event (SAE) are defined in Appendix E. All AEs, UAEs and SAEs that occur during the course of the study (until the completion of the final follow-up visit), whether observed by the investigator or by the patient, and whether or not thought to be PhotoFix related, will be reported in detail on the Adverse Event eCRF and followed to a satisfactory resolution. The investigator will follow the patient until the event resolves. In the unusual circumstance that the event has not resolved by the time of the patient's completion of the study, an explanation will be entered on the Adverse Event eCRF; the circumstance may be determined to be a permanent condition, and will be documented as such.

Secondary morbid events will not be included in the calculation of device-related complication rates. A morbid event should be documented only once unless there are multiple occurrences of that event.

Consequences of morbid events, such as explant, mortality, and reoperation will be captured on the Adverse Event eCRF, which details the associated event. In the case of an explant, additional information will be captured on the Explant eCRF (Appendix D).

Potential complications that may occur with any vascular surgery include, but are not limited to:

- Allergic reaction to medication
- Bleeding
- Breathing difficulty
- Chest pain
- Heart attack
- Infection (ex. pneumonia, urinary tract infection, wound infection)
- Irregular heartbeat
- Lung or kidney failure
- Memory loss
- Pain
- Sickness/ nausea
- Stroke
- Thrombosis

Complications specific to the use of the PhotoFix may include, but are not limited to the following:

- Abscess
- Adhesion

- Blood leakage through suture line, holes, or tears
- Calcification/mineralization
- Complete heart block (arrhythmia)
- Death
- Inflammatory immune response
- Infection
- Intimal hyperplasia
- Rejection
- Tissue damage/degradation
- Tissue failure or rupture
- Toxic response/reaction
- TSE transmission/ variant Creutzfeldt-Jakob disease

The likelihood of any complication is specific to the indication of surgery.

4.2 Consequences of Morbid Events:

Morbid events can result in mortality or the permanent cessation of all vital bodily functions. Morbid events can also require reoperation. Reoperation includes any operation that repairs, alters, or replaces a PhotoFix patch. Morbid events can also require explant. Explant includes any removal of the patch for any reason. Details on the consequences of any morbid event will be captured in the Adverse Event eCRF and Explant eCRF, as applicable (Appendix D).

4.3 Reporting Expectations

Adverse events will be reported per the following guidelines for all enrolled patients:

1. Any (potential) AE must be reported to CryoLife as soon as possible, but no later than 10 working days after knowledge of occurrence, by entry into the EDC.
2. Any UAE, SAEs or AEs of special interest (i.e. vascular complications) must be reported to CryoLife within 24 hours after gaining knowledge of the event, by email or telephone, in addition to entry into the EDC.
3. De-identified source documentation (i.e., physicians/nurse notes or summaries) regarding an AE, UAE or SAE should be provided in addition to the eCRF. The source documents can be uploaded into the eCRF (as a single file) or sent by e-mail to CryoLife.
4. Any patient death will also be reported on the Adverse Event eCRF (requested death certificate and autopsy report, if performed, should also be provided).
5. Additionally, all events shall be reported to the reviewing IRB per their reporting requirements (definitions and timelines).

Report all (potential) AE, UAE or SAE to:

Erin Hurley
Clinical Research Project Manager
CryoLife
Phone: 678-290-4627
E-mail: hurley.erin@cryolife.com

5 RISK/BENEFIT ANALYSIS

5.1 Benefits

A decellularized, photo-oxidized bovine pericardium potentially offers benefits similar to autologous pericardium (i.e., similar texture, nonimmunogenic, and biocompatible) without the disadvantages of glutaraldehyde treated tissue; the additional (not naturally-occurring) aldehyde residue from glutaraldehyde can interact with surrounding tissue, which leads to membrane damage and trapping of calcium (Ca^{2+}) on residues.[11] Design features of PhotoFix may increase the durability and functionality of the device:

- Photo-oxidation: Processing creates crosslinks and stabilizes the internal collagen structure, while eliminating toxic by-products that create sites where calcium can bind to the tissue.

The calcification potential of glutaraldehyde-fixed bovine pericardium is well known.[12,13] Preclinical results have shown that PhotoFix implanted in a cardiac sheep model demonstrated no evidence of collagen degradation, thrombogenicity, infection, excessive inflammation or intrinsic calcification in the 20-week follow-up period. PhotoFix may have enormous potential for clinical use. The long-term benefits of the unique features of PhotoFix are currently hypothetical.

5.2 Risks

Risks and complications related to vascular surgery are extensively documented in the medical literature. Complications specific to the use of PhotoFix may include, but are not limited to, the following: abscess, adhesion, blood leakage through suture line/holes/tears, calcification /mineralization, complete heart block (arrhythmia), death, inflammatory immune response, infection, intimal hyperplasia, rejection, tissue damage /degradation, tissue failure /rupture, toxic response/reaction, and TSE transmission/ variant Creutzfeldt-Jakob disease. The likelihood of each event is dependent on the specific surgical indication.

5.3 Minimization of Foreseeable Risks

Each physician must consider all the risks and benefits to the patient on an individual basis, when choosing a vascular patch. Efforts will be made to minimize these risks by selecting Investigators who are experienced in vascular surgery. In addition, efforts will be made to ensure that the treatment and follow-up of all patients will be consistent with current medical practice.

All procedures will be performed on patients who are candidates for vascular surgery, requiring the use of a patch. Patients will be carefully monitored throughout the follow-up period and any complications related to the study will be documented and evaluated.

6 DATA COLLECTION

All data will be entered by site personnel into an electronic data capture (EDC) system, (ArisGlobal) which will utilize eCRFs. The Investigator at the site will be expected to review

and approve eCRFs. All data will be subject to source document review by the Sponsor's (CryoLife) personnel or its representatives. Any corrections made to the eCRFs will be done so by a designated study coordinator or Investigator.

The eCRFs and patient's corresponding medical records (source documents) are to be fully available for review by the Sponsor's representatives at the scheduled site visits. These reviews verify adherence to the study protocol and data accuracy in accordance with federal regulations. All related electronic records at this site are subject to inspection by the Sponsor, its agents, and regulating authorities.

In accordance with ICH E6, Section 6.10, source documents include, but are not limited to the following:

- Clinic, office, hospital charts;
- Copies or transcribed health care provider notes which have been certified for accuracy after production;
- Recorded data from automated instruments such as Interactive Voice-response Systems, x-rays, and other imaging reports, e.g., Duplex Ultrasound (DUS), sonograms, CT scans, magnetic resonance images, and radioactive images (regardless of how these images are stored, including microfiche and photographic negatives);
- Correspondence regarding a study patient memorandum sent to IRB(s).

6.1 Study Endpoints & Variables

In the case of CEAs, the primary endpoint of the study will be rate of ipsilateral central neurologic events.

- Ipsilateral central neurologic events: Transient ischemic attack, amaurosis fugax, stroke, and symptomatic carotid occlusion.

In the case of all other (non-CEA) vascular procedures, the primary endpoint of the study will be primary patency in the target artery or vein.

- Primary patency (of target vessel): Loss of patency will be determined by the loss of previously palpable pulses, patients presenting with recurrent symptoms, a drop in ABI>0.15 in the case of lower limb artery repair, Doppler ultrasound findings of occlusion, angiography of the affected vessel or a combination of these.

The secondary endpoints of the study will include: overall survival rate, all-cause reoperation rate, device-related reoperation rate, explant rate, restenosis rate, adverse event rate, and secondary patency (HAR only).

- Overall Survival:
  - Early mortality: Death < 30 days following PhotoFix implantation.
  - Late mortality: Death ≥ 30 days following PhotoFix implantation, until last day of follow-up.
- All-Cause Reoperation Rate: The total number of reoperations required in patients over the follow-up period, which include the repair or alteration of the surgical area around the patch.

- Device-Related Reoperation Rate: The total number of unplanned reoperations required in patients over the follow-up period, which are determined by the surgeon to be device-related.
- Explant Rate: The total number of device explants over the course of follow-up. Explants will include the removal of PhotoFix for any reason after implantation.
- Restenosis Rate: The total number of documented cases of stenosis documented as the recurrence of abnormal narrowing of a vessel after corrective surgery.
- Adverse Event Rate: The total number of any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a device, whether or not related to the device.
- Secondary Patency (HAR only): The time from implantation to the point where the access is abandoned.

Statistical analysis will be used to assess all study endpoints as applicable.

6.2 Records and Reporting

The Investigator must maintain adequate records for the study including, without limitation, access to original source documents, medical records, laboratory reports, signed informed consent forms, adverse event reporting to the Sponsor, information regarding patients who no longer choose to be in the study or were withdrawn, all correspondence with the IRB and/or Privacy Board and CryoLife, and other pertinent data.

Data will be collected within eCRFs designed specifically for this study.

6.3 Electronic Case Report Forms

The clinical data collected for the study will be obtained from patient records, source documents, and existing databases and reported to the sponsor via eCRFs, within the electronic database. Data variables to be obtained are outlined in Appendix D and are organized by eCRF. All data collected must be supported by source documents. Patient medical records, hospital charts, operative reports, laboratory and diagnostic testing results, office visits, and other relevant documents are to be utilized for collection of relevant data. The general time points for data collection include pre-operative screening, during/ immediately following the operation, and post-operative follow-up visits (Table 2). The electronic database will store all data within the following eCRFs: Informed Consent, Eligibility Evaluation, Baseline Assessments (Demographics, Medical History, Surgical History, and Social History), Imaging Evaluation, Medication, Operative Assessment, Follow-Up Evaluation, Adverse Event, Explant Evaluation, and End of Study.

6.4 Data Reporting

All data will be entered by site personnel into eCRFs. The Investigator at the site will be expected to review and approve eCRFs. Any corrections made to the forms at a study site will be done so by a designated study coordinator (or Investigator). Form changes will be tracked in the EDC.

6.5 Data Review

The completed eCRFs will be reviewed for completeness and clarity by the Sponsor's data manager and the Sponsor's representative clinical research associates. Throughout the study, the data manager and clinical research associates will issue queries for any information inadvertently omitted, inconsistent, not supported by source documents, or not answered within the EDC. The data manager may request further documentation when data issues, complications, device malfunctions, or explants are observed and reported. The site will be responsible for clarification and resolution of all queries. The data manager will close queries after sufficient clarification and resolution is achieved.

6.6 Data Quality Control

Site investigators will sign off on all study forms prior to data lock. Additionally, data will be 100% source document verified by the Sponsor or a representative of the Sponsor, as deemed necessary.

6.7 Statistical Analysis Plan

Enrolled patients will be described in aggregate and by indication (as deemed appropriate); baseline characteristics will include, but not limited to, age, sex, race, ethnicity, body mass index (BMI), comorbidities, fundamental diagnosis/etiology, and pertinent surgical history. Operative details will be described in aggregate and include a summary of the types of procedures performed, by relevant category. Parameters with continuous data types will be summarized using descriptive statistics, i.e., mean, standard deviation, and range. Categorical clinical parameters will be summarized based on percentages.

Ipsilateral central neurologic event rate, overall survival, re-operation rate, explant rate, and restenosis rate (≥ 50% stenosis) will be summarized based on percentages of affected patients and included in a table, which will summarize the endpoints in aggregate and by surgical indication (ex. CAS, ESRD, PAD, AAA, etc.). The summary of ipsilateral central neurologic event rates will include all events (transient ischemic attack, amaurosis fugax, stroke, and symptomatic carotid occlusion), as well as the incidence of each event individually.

Additional analysis of follow-up data will also be performed with the Kaplan-Meier method, as deemed appropriate by the incidence of events. Kaplan-Meier plots may be generated for endpoints including overall survival, primary patency, secondary patency, as well as freedom from ipsilateral central neurologic event rate, re-operation, explant, and restenosis (≥ 50% stenosis). Kaplan-Meier plots for survival will include the following mortality classifications: all causes of mortality, vascular-related mortality and device-related mortality (as applicable). The remaining plots will be specific to indication, if the sample sizes allow for the creation of meaningful plots.

The incidence of adverse events will be categorized and summarized with percentages for the aggregate sample. Adverse events will be divided into early and late post-operative events to represent the distribution of occurrences. Events will be considered as early events if the event occurs <30 days after the operation, while late post-operative events will be considered to be all events happening after this time period. Early and late events will be presented by indication for surgery, seriousness of event, and relation to PhotoFix. Adverse events occurring secondary to

another complication will be collected, but not included in the calculation of adverse event rates. Adverse events occurring prior to PhotoFix implant will not be reported.

An interim analysis of the data will be performed approximately 6 months after the initiation of enrollment. The sample size will be dependent on enrollment rate; follow-up could range from 0 days to 5 months. This analysis will be used to assess the interim performance and safety of PhotoFix. The analysis of this data will also be used to address the planned enrollment of the study and to determine if any modifications to the study are necessary.

6.8 Privacy of Patient Data & Patient De-identification

All patient data will remain confidential. Patient names, social security number, addresses, or any other identifying information will not be reported. Patients and their data will be de-identified with the use of a Screening ID. Patients will sign a HIPAA waiver acknowledging that their information will remain confidential. The sample HIPAA waiver is attached in Appendix A.

The site will be provided with a patient log that they will use to record the Screening ID and patient information at the time of each screening. The site is responsible for maintaining the log. The unique 4-digit Screening ID will be assigned per the following scheme: the first two digits are the site assigned abbreviation, followed by the sequential number in which the patient was consented.

Example: The 1st patient screened at site CR

Site (2 letter)		Patient Enrolled (2 digit)	
C	R	0	1

6.9 Record Maintenance

All correspondence related to this study should be kept in appropriate study files. Patient records, source documents, and IRB and Sponsor correspondence pertaining to the study must, be kept on file.

7 SITE MANAGEMENT PLAN AND MONITORING

It is the responsibility of CryoLife to ensure proper management of the clinical study. Frequency of site visits will be determined by any of the following criteria: patient volume at a site, site compliance with the study protocol, and study duration. Site visits may be completed in person or remotely. One hundred percent source document verification (SDV) is intended for this study. Exceptions to this monitoring goal will include screen failures. One hundred percent SDV for screen failures will be restricted to the following eCRFs: Informed Consent, Eligibility Evaluation, and Demographics.

Study management will be performed by appropriately trained personnel appointed by the Sponsor and will be documented per standard operating procedures (SOPs) to ensure that the clinical study is conducted in accordance with:

- The signed Investigator Agreements
- The protocol
- Food and Drug Administration (FDA) regulations (as applicable) and Good Clinical Practice (GCP)

8 PATIENT WITHDRAWAL

At the discretion of the physician, a patient can be removed from the study at any time without the patient's consent for the following reasons: a) it is in the best interest of the patient to be withdrawn from the study; b) patient non-adherence to the study protocol requirements; c) patient, sponsor or investigator request; d) the investigator may also elect to withdraw the patient from the study at any time based on their medical judgment.

A patient will be considered Lost to Follow-up and therefore terminated from the study when the following criteria are met: failure to complete two consecutive follow-up visits (without due cause) AND documentation of three unsuccessful attempts by the investigator or his/her designees to contact a patient or next of kin, including at least one registered letter.

Subjects who request discontinuation from the study prior to completion will be encouraged to complete their study follow-up visits, particularly the 6-month visit; at a minimum, the patients can be followed per protocol for safety.

It is the responsibility of the treating physician to notify the Sponsor of any patients removed from the study.

9 DEVIATION FROM PROTOCOL

If a protocol deviation occurs, notifications to the Sponsor must be made within 10 working days of the occurrence of a deviation. Details of the deviation must be documented in writing and provided to CryoLife with a copy maintained in the Investigator's file. All deviations must be documented on the provided Protocol Deviation Form (Appendix G). If the deviation affects the rights, safety or welfare of the patients (and it is not an emergency), or the scientific soundness of the investigation, prior approval must be obtained from CryoLife, the reviewing IRB, and FDA or applicable Regulatory Authorities (when required). For all other deviations, prior approval must be obtained from CryoLife.

10 STUDY REPORT

CryoLife will generate a final study report within 4 months after termination or completion of the clinical study.

11 STUDY ADMINISTRATION

11.1 Institutional Review Board Information

The Investigator is responsible for submitting the appropriate study documentation to the Institutional Review Board (IRB) for review and approval in accordance with federal regulations. A copy of the written approval for the protocol and informed consent form must be submitted to Sponsor before patient enrollment can begin. The Investigator will be held responsible for keeping the IRB informed of all significant findings throughout the course of the study. The Investigator will be required to notify the IRB in accordance with the Board's written procedures if any of the following should occur:

- Amendments to the protocol or informed consent form.
- Safety updates generated by the Sponsor.
- UAE, SAEs and AEs (See Appendix E) of special interest must be reported to the Sponsor within 24 hours of a site first becoming aware of an event, and additionally to the IRB per their reporting guidelines.
- Any deviations from the protocol.
- Any information related to patient safety.

11.2 Patient Informed Consent

All patients must voluntarily provide signed informed consent, prior to the collection of prospective assessments, which would not have been performed as part of normal patient care. Informed consent must be obtained in accordance with the FDA regulation 21CFR Part 50 (see Appendix B). Prior to obtaining written consent, the Investigator or delegate must give each patient a written explanation of the study. This must be accompanied by a verbal explanation, including the purpose and nature of the study, potential benefits and risks, and patient rights as a study participant. Adequate time must be allowed for each patient to consider the diagnostic and treatment options and to ask questions. The Investigator will retain the original signed consent form, which must be made available for review by interested parties. A copy will be made available to each patient.

Informed consent forms must be approved prior to the study initiation by both the IRB and CryoLife. The informed consent form must be written in language readable to each patient. A sample informed consent form is attached in Appendix B.

11.3 Publication Policy

The conduct and results of this study will be documented in study reports prepared by CryoLife, or a representative of CryoLife, in accordance with SOPs. It is intended that the clinical results from this study will be published and/or presented at a scientific forum. The Investigator will not publish or present results without prior consent from CryoLife. Additionally, CryoLife reserves the right to future discussions with the Investigator including, but not limited to, continuance of current study and/or combining the study data with other data series with the intent of creating a multi-center evaluation of PhotoFix. The study will be registered on https://www.clinicaltrials.gov.

11.4 Confidentiality

This protocol is a confidential communication of CryoLife. Acceptance of this document constitutes the agreement by the recipient that no unpublished information contained within will be published or disclosed without prior written approval, except that this document may be disclosed to the IRB under the condition that it is requested that they keep it confidential.

The privacy of patients who participate in this study will be protected by all reasonable means. The Principal Investigator is responsible for study records at study sites. Access to study records, and especially patient information, will be limited to the Investigator, the Sponsor and its representatives, and Regulating Bodies.

APPENDIX A: HIPPA

Confidentiality

While you are in this study, information about you and your progress will be kept in a private file by your study doctor, and a private file at the corporate headquarters of CryoLife. The privacy of patients or patients who participate in this study will be protected by all reasonable means. During the reviews, representatives or designees of CryoLife, <<Insert Investigator Name>> and members of the support staff and clinical team, U.S. Food and Drug Administration (FDA), and Sterling Institutional Review Board may have access to medical records that contain your identity. However, no information by which you can be identified will be released or published. Your file will be kept as private as the HIPAA law allows.

Data Privacy – Confidentiality – Authorization to Disclose Health Information

Release of Health Information – If you decide to participate in this study, information about your health may be used or disclosed for the purposes of conducting this study. This information may include information from your medical record that is relevant to this study, such as your medical history, medications, test results, diagnoses, treatments, operative reports (reports from operations that you have undergone), and discharge summaries. Information collected by the study doctor and/or research staff specifically for this study, such as test results, blood samples, physical examinations, information about possible side effects, and surveys you might be asked to complete could also be used or disclosed.

Individual's that may use or release this information include: physician's, physician's office staff, hospital staff, the study doctor, and authorized members of the study doctor's research staff. These individual's may release this information to the study doctor, authorized members of <<Insert Investigator Name>>staff, the sponsor (CryoLife) of the study, sponsor's agents and representatives, Sterling, FDA representatives, and other regulatory agencies.

The information released to the above listed individuals will not contain your name, social security number, or any other personal information. However, authorized representatives of the sponsor, IRB, FDA or other regulatory agencies may review records containing personal information that can identify you, to make sure that the study information is correct. Because of the need to provide information to these parties, absolute confidentiality cannot be guaranteed.

Use of Information – This information may be used to monitor your healthcare during the study, to enable the sponsor to answer the scientific questions for which the study was designed, and to ensure that the study has been done properly. Examples of the use of this information are as follows: the sponsor may use the information for reporting adverse events to regulatory agencies, such as the FDA; the sponsor may also transfer the information to business partners or companies it hires to provide study-related services; both the sponsor and the study doctor may use the information to prepare reports or publications of the study results; the sponsor may also provide overall study results, including your information, to other study doctors; the sponsor may reanalyze the data from this study in the future or combine it with data from other studies for analysis.

Once your information has been released, it is no longer protected by US federal regulations relating to data privacy and could be used or re-disclosed in ways other than those listed in this section of the consent form.

You have the right to see and receive a copy of your records related to the study for as long as the study doctor has this information in his/her possession. However, you might not be allowed to see these records until after the study has been completed.

Authorization to Disclose – By signing this consent form, you authorize disclosure of information to the sponsor and review of your medical records by the sponsor and other authorized people, as described in this section of the consent form. You do not have to authorize this disclosure of information. However, if you do not, you will not be able to participate in this study.

Expiration of Authorization – Because this information is being disclosed for research use, there is no expiration date for the authorization to disclose and use this information. The sponsor may keep and continue to use your study information for many years. Your study doctor may need to add to or correct information about you even after your study participation is over, including providing updates of your health status if that is important to the purpose of the study. The review of your medical records (discussed above) may also take place after the study is over. This authorization will remain in effect unless you revoke it.

Revoking Authorization to Disclose – If you stop participating in this study, you also have the right to revoke (withdraw) your authorization to disclose information. Revoking your authorization means taking back the permission you gave the study doctor to send information about you to the sponsor. If you revoke your authorization, your study doctor will not use or release any more information about you after receiving your request, except to tell the sponsor that you have stopped early and have revoked your authorization. However, the sponsor can still keep and use any information that it has already received.

You may revoke your authorization at any time. However, once you do so, you can no longer continue to participate in the study.

If you want to revoke your authorization, you must do so in writing to the study doctor. You can get a revocation form from your study doctor or you can write a letter to the study doctor.

STUDY: Evaluation of PHOTO-Oxidized Decellularized Bovine Pericardium as a Patch in Vascular Repair and Reconstruction Surgery (PHOTO-V)
PROTOCOL NO: PHF1801.000-M (04/18)
STERLING IRB ID: «IRB_ID»

PARTICIPANT INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE MEDICAL INFORMATION

STUDY TITLE: Post-market, prospective evaluation of PHOTO-oxidized decellularized bovine pericardium used as a patch in Vascular repair and reconstruction surgery: PHOTO-V

PROTOCOL NO: PHF1801.000-M (04/18)

STUDY DOCTOR: «First_Name» «Middle_Name» «Last_Name», «Suffix»

STUDY SITE: «Company_Name»
«Address»
«City_State_ZIP»

TELEPHONE: «Telephone»
«Telephone_2_if_applicable»

SPONSOR: Cryolife, Inc.

You are being asked to volunteer to take part in a research study. Before choosing to be part of this study, you should read this consent form. This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. It describes the possible risks and benefits that could happen to you if you choose to take part in this study. It explains the other choices you have besides taking part in this study. This form also explains your right to stop taking part in the study at any time.

This consent form may contain words or information that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form if you wish to think about or discuss this consent form with family or friends before making your decision. After thinking about all the written information given to you, as well as your discussion with the study doctor and his or her study staff, you may decide you want to take part in the research study. If so, you will be asked to sign this consent form for yourself and a copy will then be given to you.

BACKGROUND

You are being asked to take part in this study because you need a vascular surgery, which requires patch material to close or repair defects in blood vessels. PhotoFix® is a patch used for vascular surgeries.

PhotoFix® is considered a medical device and is made from sterilized bovine pericardium (the tough tissue sac that surrounds the heart of a cow. None of the procedures or evaluations related to the study are investigational. PhotoFix® is approved for use in the United States (US)

STUDY: Evaluation of PHOTO-Oxidized Decellularized Bovine Pericardium as a Patch in Vascular Repair and Reconstruction Surgery (PHOTO-V)
PROTOCOL NO: PHF1801.000-M (04/18)
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by the FDA as a device. PhotoFix® (previously named CardioFix) has been sold in the US since 1999.

PhotoFix® is made by the sponsor of this study, CryoLife, a company located in Kennesaw, Georgia.

PURPOSE OF THE STUDY

The purpose of this study is to provide additional information about how well PhotoFix® works as a patch used to complete part of your surgical procedure.

Approximately 100 men and women age 18 and older who are undergoing vascular surgical procedures will participate in this study across multiple clinical sites.

PROCEDURES

Participation in this study will last six months from your date of surgery and involves a Pre-Operative visit, Surgical Visit and three post-op follow-up appointments at 1, 3, and 6 months after surgery. The following describes the information that will be collected or procedures performed during the study.

Pre-Operative Visit: During this visit, the study doctor will determine if you are eligible to participate in the study.

- You will be asked to read and sign this consent form.
- The study doctor will ask about your medical, medication and surgical history and your demographics (for example, age, sex, race). Please be sure to inform your study doctor or study staff of any prescription medications you are taking, as well as if you smoke.
- Information about your condition including any images taken before surgery will be reviewed for research purposes.

Operative Visit: Your surgical procedure will be performed using standard of care procedures. If you qualify for the study and you wish to be included, your study doctor will use PhotoFix to complete part of your surgical procedure. When you wake up, you will be watched closely until you go home from the hospital.

Follow-Up Visits:

You will return for visits at 1 month, 3 months and 6 months after your surgery. At these checkups the following will be done:

- The study doctor or study staff will review any changes in your health, your current medications and any side effects or problems you have experienced from your surgery.
- You may have a physical exam. The physical exam will not include a pelvic, rectal, or breast exams.
- You may have an imaging procedure performed.

STUDY: Evaluation of PHOTO-Oxidized Decellularized Bovine Pericardium as a Patch in Vascular Repair and Reconstruction Surgery (PHOTO-V)
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POTENTIAL RISKS, SIDE EFFECTS, DISCOMFORTS, INCONVENIENCES

Vascular patches like the one being studied can cause complications, or problems. You need to know that your patch may cause none, some, or all of the problems listed below. It is possible that you could have very uncommon or previously unknown problems.

Your study doctor will talk to you about all of the known problems that could happen because of your condition and the procedures you will undergo as part of the study. By being in this study, you could have the same type of problems that you would have with other patches or with the procedures if done outside of the study. A major risk would be if the patch made your vascular condition worse and you needed a different treatment.

Risks and complications related to using PhotoFix® include:

- Abscess (a swollen area filled with pus)
- Adhesion (PhotoFix® attaches to other tissue near the application site)
- Blood leakage through suture lines, holes, or tears
- Calcification/mineralization (build up of calcium or other minerals at the site where the patch was applied)
- Complete heart block (arrhythmia)
- Death
- Inflammatory immune response
- Infection
- Intimal hyperplasia (thickening of the blood vessel wall)
- Rejection of the patch
- Tissue damage/degradation
- Tissue failure or rupture
- Toxic response/reaction
- Exposure to substances that might cause infection that affect the brain and nervous systems (Transmissible Spongiform Encephalopathy transmission [condition that affects the brain and nervous system, such as Creutzfeldt-Jakob disease])

Some of the problems that may be caused by PhotoFix® are inflammatory (painful) or immune (swelling) responses and allergic reactions (like getting sick from a bee sting). Because PhotoFix® is made from pieces of bovine pericardium, it is possible that you could catch a sickness from the animal.

There are no known reproductive risks associated with the procedures to be conducted during the study. There may be other known and/or unknown risks that you may wish to discuss with your study doctor.

PREGNANCY DURING RESEARCH

If you are pregnant, you cannot take part in this study. Women who are neither post-menopausal for one year nor surgically sterile will take a urine pregnancy test to determine

pregnancy status before the start of treatment. You must avoid becoming pregnant during the study. If you become pregnant after the study begins, you will not be allowed to continue.

POTENTIAL BENEFITS

If you decide to be in this study, PhotoFix® is expected to help you as much as other vascular patches would. PhotoFix® may last longer than other patches.

Your study doctor does not know if anything good will happen to you just because you decide to be in this study. You might not get any help at all by being in this study. If you do decide to be in this study, the things that researchers learn from you may help other people.

ALTERNATIVE TREATMENT

If you choose not to participate your study doctor will discuss other standard treatments for your condition, which may be using an alternative vascular patch. Other vascular patches on the market are currently available and used by other doctors for vascular surgeries like the one you need. Ask your study doctor about the risks and benefits of alternative treatments before you take part in this study.

NEW INFORMATION

If new information develops, during the course of the study, that might change your decision to be in this study, you will be told about this new information. After receiving this information, you can decide if you would like to continue participating in the study.

STUDY FUNDING

The research study is being sponsored by Cryolife, Inc.. Cryolife, Inc. is called the Sponsor and «Company_Name» is being paid by Cryolife, Inc. to conduct this study. Dr. «Last_Name» is the study doctor and is a member of the medical staff of «Company_Name».

COSTS TO YOU

The costs associated with your vascular surgery, as well as any standard of care during the study are your (or your insurance company's) responsibility, the same as if you choose not to participate in the study.

However, neither you nor your insurance company will have to pay for any procedures conducted during the study that are not traditionally covered items that would occur as an additional fee, as a result of the study protocol.

COMPENSATION TO YOU

A «Per_Visit» gift card will be provided to you to cover the cost of your travel expenses associated with attending the 1, 3, and 6 month post-operative visits. You will only be

compensated for the visits you complete. A completed visit means all required data has been collected by your study doctor.

STUDY COMPLICATIONS AND COMPENSATION

Problems can happen during a research study. These problems may not be your fault, or your study doctor's fault, the study sponsor's fault, nor caused by PhotoFix®. If you are hurt because you are in this study, your study doctor will take care of you. If you have a medical emergency and you have followed the directions of your study doctor or other study personnel and CryoLife decides that emergency is related to PhotoFix®, Cryolife, Inc. will pay for needed emergency care not covered by your insurance. Cryolife, Inc. has set aside no other compensation. Cryolife, Inc. has no plans to make payments for things like lost income or emotional distress. If you are injured as a result of this study, you do not give up your right to pursue a claim through the legal system.

If you have concerns about your insurance coverage, you may want to contact your insurance carrier. Your health insurance company may or may not pay for treatment of injuries as a result of your participation in this study.

VOLUNTARY PARTICIPATION/WITHDRAWAL

Your participation in this study is voluntary. You may decide not to participate or you may choose to be removed from the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled, and your doctor will still take care of you.

The study doctor in charge of this study or the sponsor can remove you from the study at any time without your consent for the following reasons:

- it is in your best interest to be withdrawn from this study
- you do not follow the study instructions and/or study schedule
- the study is stopped early
- you do not consent to continue in the study after being told of changes in the research that may affect you
- you become pregnant
- or for any other reason

The sponsor of the study or Sterling IRB can also stop the study at any time. You can decide to see another doctor at any time if you want to. If you agree to participate in this study and you sign this consent form, you still may be withdrawn from the study against your wishes for any of the following reasons: undue risk or injury or reaction.

CONFIDENTIALITY

Information obtained about you for this study will be kept private to the extent allowed by law. Information about you and your progress will be kept in a private file by your study doctor and corporate headquarters of Cryolife, Inc.. Research information that identifies you may be shared

with the Sterling Institutional Review Board and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of Cryolife, Inc., the U.S. Food and Drug Administration (FDA),and the Office of Human Research Protections (OHRP). However, no information by which you can be identified will be released to the public or published, unless required by law. However, as described below certain individuals and institutions may review records containing personal information to make sure that the study information is correct and the study is being conducted as required by law.

DATA PRIVACY – CONFIDENTIALITY – AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Release of Health Information

If you decide to participate in this study, information about your health may be used or disclosed for the purposes of conducting this study. This information may include information from your medical record that is relevant to this study, such as your medical history, medications, test results, diagnoses, treatments, operative reports (reports from operations that you have undergone), and discharge summaries. Information collected by the study doctor and/or research staff specifically for this study, such as test results, blood samples, physical examinations, information about possible side effects, and surveys you might be asked to complete could also be used or disclosed.

Individuals that may use or release this information include: physicians, physicians' office staff, hospital staff, the study doctor, general practitioners, and authorized members of the study doctor's research staff. These individuals may release this information to the study doctor, authorized members of the study doctor's study staff, Cryolife, Inc. and its representatives working on behalf of Cryolife, Inc., Sterling Institutional Review Board and U.S. FDA.

The information released to the above-listed individuals will not contain your name, Social Security Number, or any other personal information. However, authorized representatives of the sponsor, Sterling Institutional Review Board, or U.S. FDA may review records containing personal information that can identify you to make sure that the study information is correct. Because of the need to provide information to these parties, absolute confidentiality cannot be guaranteed.

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

Use of Information

Information may be used to determine whether you meet all requirements for participation in the study, to monitor your healthcare during the study, to enable the sponsor to answer the scientific questions for which the study was designed, and to ensure that the study has been done properly. Examples of the use of this information are as follows:

- Cryolife, Inc. may use the information in submissions to regulatory agencies throughout the world
- Cryolife, Inc. may use the information for reporting adverse events to regulatory agencies, such as the U.S. FDA
- Cryolife, Inc. may also transfer the information to business partners or companies it hires to provide study-related services
- Both Cryolife, Inc. and the study doctor may use the information to prepare reports or publications of the study results
- Cryolife, Inc. may also provide overall study results, including your information, to other study doctors
- Cryolife, Inc. may reanalyze the data from this study in the future or combine it with data from other studies for analysis

Once your information has been released, it is no longer protected by U.S. federal regulations relating to data privacy and could be used or re-disclosed in ways other than those listed in this section of the consent form.

You have the right to see and receive a copy of your records related to the study for as long as the study doctor has this information in his possession. However, you might not be allowed to see these records until after the study has been completed.

Authorization to Disclose

By signing this consent form, you authorize disclosure of information to the sponsor and manufacturer (Cryolife, Inc.) and review of your previous medical records by the sponsor as described in this section of the consent form. You do not have to authorize this disclosure of information. However, if you do not, you will not be able to participate in this study.

Release of Photographic Data Collection

De-identified images, including photographs and stills from diagnostic evaluations, of your arteries/veins may also be collected during follow-up. These images will not reveal your identity. These images will be used as visual documentation of the status of PhotoFix and your vasculature and may be used in scientific publications, for educational purposes, and in sponsor's promotional and marketing materials, such as brochures, website material and advertising. By signing this consent form, you voluntarily authorize disclosure of the de-identified images or videos to the sponsor and manufacturer, Cryolife, Inc., for Cryolife, Inc.'s (or Cryolife, Inc.'s authorized representative's) use as described in this section of the consent form. You also agree and acknowledge that you do not expect to be compensated in any fashion related to the use of such images or videos and voluntarily release sponsor from any claims or damages that result from sponsor's use of the images or videos.

Expiration of Authorization

Because this information is being disclosed for research use, there is no expiration date for the authorization to disclose and use this information. The sponsor may keep and continue to use

your study information for many years. Your study doctor may need to add to or correct information about you even after your study participation is over; including providing updates of your health status if that is important to the purpose of the study. The review of your medical records (discussed above) may also take place after the study is over. This authorization will remain in effect unless you revoke it.

Revoking Authorization to Disclose

If you stop participating in this study, you also have the right to revoke (withdraw) your authorization to disclose information. Revoking your authorization means taking back the permission you gave the study doctor to send information about yourself to the sponsor. If you revoke your authorization, your study doctor will not use or release any more information about you after receiving your request, except to tell the sponsor that you have stopped early and have revoked your authorization. However, the sponsor can keep and use any information that they have already received. You may revoke your authorization at any time. However, once you do so, you can no longer continue to participate in the study.

If you want to revoke your authorization, you must do so in writing to the study doctor. You can get a revocation form from your study doctor or you can write a letter to the study doctor.

QUESTIONS

If you have questions, concerns or complaints about the research study or you experience a research-related injury, please contact Dr. «Last_Name» or the study staff at «Telephone» or «Telephone_2_if_applicable».

If you have questions regarding your rights as a research participant, or if you have questions, concerns, complaints about the research, would like information, or would like to offer input, you may contact the Sterling Institutional Review Board Regulatory Department, 6300 Powers Ferry Road, Suite 600-351, Atlanta, Georgia 30339 (mailing address) at telephone number 1-888-636-1062 (toll free).

Sterling is a group of people who perform independent review of research studies to ensure that they are conducted in accordance with applicable laws. Sterling will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact Sterling if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

STUDY: Evaluation of PHOTO-Oxidized Decellularized Bovine Pericardium as a Patch in Vascular Repair and Reconstruction Surgery (PHOTO-V)
PROTOCOL NO: PHF1801.000-M (04/18)
STERLING IRB ID: «IRB_ID»

PARTICIPANT STATEMENT AND AUTHORIZATION

I have read the Participant Informed Consent Form and Authorization to Use and Disclose Medical Information and I agree to participate voluntarily in this study. I give my permission to the study doctor to use and disclose my protected health information as described in this consent form.

I will receive a signed copy of this form, which has 9 pages. All my questions have been answered. I have not waived any of my legal rights by signing this document.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of Person Explaining Consent

_____ _____
Signature of Person Explaining Consent (if other than the Principal Investigator) Date

_____ _____
Signature of Principal Investigator Date

Internal Use Only

Assigned Subject ID: ___ ___ ___ ___

APPENDIX C: IFU

PhotoFix®

Decellularized Bovine Pericardium

QTY 1

Quantity

INSTRUCTIONS FOR USE

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

DEVICE DESCRIPTION

PhotoFix® Decellularized Bovine Pericardium (PhotoFix) is prepared from bovine pericardium, which is stabilized using a dye-mediated photooxidation process, processed using ethylene oxide and sterilized using aseptic processing techniques. No aldehyde chemistry is used during any phase of pericardium manufacturing including tissue fixation or sterilization processes.

INDICATIONS

PhotoFix is indicated for the following uses: intracardiac repair, great vessel repair, suture line buttressing, pericardial closure, and vascular repair and reconstruction (for example: the carotid, iliac, femoral, and tibial blood vessels and arteriovenous access revisions).

CONTRAINDICATIONS

PhotoFix is contraindicated for:

- Use in patients that exhibit sensitivity to materials of bovine origin;
- Reconstruction of hernias and valve leaflet repair.

WARNINGS AND PRECAUTIONS

- FOR SINGLE USE ONLY
- PhotoFix is supplied sterile in a sealed container. Do not re-sterilize.
- Do not use the pericardium if either temperature indicator is activated (see TEMPERATURE INDICATORS section). Immediately contact your Sales Representative to arrange for return or replacement of the tissue.
- DO NOT USE THE PERICARDIUM if the device container is damaged, the expiration date has lapsed, or the tamper-evident seal is broken or missing.

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- PhotoFix should not be allowed to contact any solutions that contatin aldehydes.
- Rinsing the pericardium with antibiotic solution is not recommended. The interactions of tissue with antibiotics have not been tested.

ADVERSE EVENTS

Potential adverse events associated with the use of pericardium include: Abscess, adhesion, calcification/mineralization, complete heart block, death, epicardial inflammatory reactions, infection and rejection.

Adverse events potentially related to the product must be reported promptly to CryoLife Field Assurance at 1-800-438-8285 or 770-419-3355 or by email to fieldassurance@cryolife.com.

INDIVIDUALIZATION OF TREATMENT

Prophylactic antibiotic therapy is necessary for patients that receive an implantable device when undergoing any invasive procedure (including and especially dental procedures).

PATIENT COUNSELING

Patients undergoing any dental procedures should be considered for prophylactic antibiotic therapy.

HOW SUPPLIED

PhotoFix is supplied sterile and non-pyrogenic in a sealed container with 22% buffered ethanol solution. After implantation, the 22% buffered ethanol solution can be discarded according to hospital procedures for non-hazardous materials.

TEMPERATURE INDICATORS

Each shipping carton contains low and high temperature indicators that signify if the tissue was exposed to unacceptable shipping temperatures. If the background of the low temperature indicator is **RED**, the product was exposed to temperatures below the acceptable shipping temperature (**Figure 1**). If the high temperature indicator is **RED**, the product was exposed to temperatures above the acceptable shipping temperature (**Figure 2**).

Figure 1

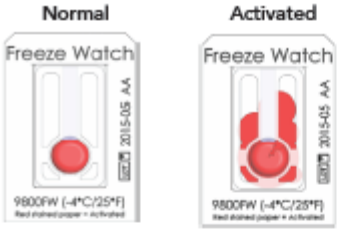

Figure 2

If either high or low temperature indicators have been activated, DO NOT USE THE PERICARDIUM. Immediately contact your Sales Representative to make arrangements for return or replacement.

STORAGE CONDITIONS

PhotoFix should be stored between the temperature limit minimum of 5°C and maximum of 25°C (41°F and 77°F). Refrigeration is not required. Do not place PhotoFix in areas where significant temperature fluctuations may occur.

DIRECTIONS FOR USE

1. The exterior of the container is non-sterile and should not be introduced into the sterile field.
2. Remove the tamper-evident seal by pulling tab adjacent to the seal perforation.
3. Grip the bottle lid and open the container by turning the lid counterclockwise.
4. Remove PhotoFix from the container by grasping the edge of the pericardium with atraumatic forceps. ATRAUMATIC FORCEPS MUST BE USED WHEN HANDLING PHOTOFIX. Alternatively, the tissue and bottle contents can be poured into a sterile basin.
5. PhotoFix does not require rinsing before implantation.
6. All subsequent handling must be with sterile gloved hands. Thoroughly wash surgical gloves to remove glove powder before touching the pericardium.
7. PhotoFix may be tailored during surgery as needed. The pericardium may be sutured, clipped, or stapled into place.
8. Flush the pericardium with sterile physiologic saline frequently during implantation to prevent tissue dehydration.

WARRANTIES

THE FOLLOWING DISCLAIMER OF WARRANTY APPLIES TO UNITED STATES CUSTOMERS ONLY: ALTHOUGH THE CRYOLIFE, INC. PHOTOFIX® DECELLULARIZED BOVINE PERICARDIUM, HEREAFTER REFERRED TO AS "PRODUCT", HAS BEEN DESIGNED, MANUFACTURED AND TESTED UNDER CAREFULLY CONTROLLED CONDITIONS, DUE

TO CONDITIONS AND FACTORS THAT ARE OUTSIDE OF CRYOLIFE, INC.'S SUPERVISION AND CONTROL AFTER SALE OF THE PRODUCT, CRYOLIFE, INC. HEREBY DISCLAIMS ALL WARRANTIES EXPRESSED OR IMPLIED WITH RESPECT TO THE PRODUCT, INCLUDING BUT NOT LIMITED TO ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. CRYOLIFE, INC. SHALL NOT BE LIABLE TO ANY PERSON OR ENTITY FOR ANY DIRECT, INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL OR OTHER TYPE OF DAMAGES INCLUDING, WITHOUT LIMITATION, ANY MEDICAL EXPENSES CAUSED BY OR RELATED TO ANY USE, DEFECT, FAILURE OR MALFUNCTION OF THE PRODUCT, WHETHER BASED UPON A WARRANTY, CONTRACT, TORT OR OTHER LEGAL THEORY. CRYOLIFE, INC. NEITHER ASSUMES, NOR AUTHORIZES ANY OTHER PARTY TO ASSUME FOR IT, ANY WARRANTY, REPRESENTATION OR OTHER LIABILITY IN CONNECTION WITH THE PRODUCT OR ITS USE.

If any term or portion of this Disclaimer of Warranty and Liability provision is found to be unenforceable, illegal or contrary to applicable law by a court of competent jurisdiction, the remaining portions of this provision shall not be effected and shall remain valid, and any such unenforceability or illegality in jurisdiction shall not invalidate or render unenforceable this Disclaimer of Warranty and Liability provision in any other jurisdiction.


Manufacturer

CryoLife, Inc.
1655 Roberts Blvd., NW
Kennesaw, GA 30144
Telephone: 800-438-8285
Fax: 770-590-3753

L09154.001 (12/2017)

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APPENDIX D: DATA VARIABLES (BY FORM)

Informed Consent eCRF	
Subject ID	
1. Subject was fully informed regarding the study.	☐ Yes ☐ No
2. The consent form was signed and dated by the subject prior to any study procedures.	☐ Yes ☐ No
3. Subject was given a copy of the signed consent form.	☐ Yes ☐ No
ICF Version Date:	_____/_____/_____ Month/Day/Year
4. HIPPA was obtained.	☐ Yes ☐ No
5. Date Informed Consent and HIPPA forms signed by subject:	_____/_____/_____ Month/Day/Year
6. Informed Consent and HIPPA obtained by (Full Name):	
*If any question is answered "No", a detailed explanation must be provided. The subject must be contacted immediately and consent process completed prior to any further study procedures being completed.	

Eligibility Criteria eCRF	
Study Subject ID	
Date of Screening:	____/____/_____ Month/Day/Year
Inclusion Criteria	
1. Patient is undergoing a vascular procedure which falls within the indications for use and requires the use of PhotoFix Decellularized Bovine Pericardium.	☐ Yes ☐ No
2. Patient's surgery is anticipated to occur within 60 days of consent.	☐ Yes ☐ No
3. Patient is ≥18 years old.	☐ Yes ☐ No
4. Patient is willing and able to comply with the protocol and follow up period.	☐ Yes ☐ No
5. Patient is willing and able to give written informed consent.	☐ Yes ☐ No
Exclusion Criteria	
6. Patient's procedure is a revision of a prior arteriotomy or venotomy.	☐ Yes ☐ No
7. Patient's procedure requires multiple vascular patches in anatomically distinct regions or other prosthetics (e.g. stents).	☐ Yes ☐ No
8. Patient has a medical history of abnormal coagulopathy, bleeding, or thromboembolic disease.	☐ Yes ☐ No
9. Patient has a medical history of severe immunodeficiency disease.	☐ Yes ☐ No
10. Patient has a medical history of cancer.	☐ Yes ☐ No
11. Patient has severe visceral disease affecting the heart or active liver disease or icterus.	☐ Yes ☐ No
12. Patient has a history of cerebrovascular accident (completed stroke) within 3 months of planned surgery.	☐ Yes ☐ No
13. Patient has a history of atrial fibrillation and requires a patch for carotid endarterectomy repair.	☐ Yes ☐ No
14. Patient has an active or potential infection at the surgical site.	☐ Yes ☐ No
15. Patient has used or plans to use immunomodulatory drugs for ≥ 6 months.	☐ Yes ☐ No
16. Patient has a sensitivity to products of bovine origin.	☐ Yes ☐ No
17. Patient is currently enrolled in another study.	☐ Yes ☐ No
18. Patient has a life expectancy of less than 12 months.	☐ Yes ☐ No
19. Patient is pregnant or breastfeeding or planning on becoming pregnant or unwilling to use medically acceptable methods of birth control.	☐ Yes ☐ No
20. Patient's procedure is emergent.	☐ Yes ☐ No
Does the patient meet all inclusion and exclusion criteria and can be considered eligible for enrollment?	☐ Yes ☐ No

Demographics eCRF	
Study Subject ID	
1. Date of Birth	_____/_____/_____ Month/Day/Year
2. Sex	☐ Male ☐ Female
3. Race	☐ American Indian or Alaska Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian or Pacific Islander ☐ White ☐ Unknown (select all that apply)
4. Ethnicity	☐ Non-Hispanic ☐ Hispanic ☐ Unknown
5. Height (inches)	☐ Unknown
6. Weight (lbs)	☐ Unknown

Medical History eCRF	
Study Subject ID	
1. Indication for Surgery	☐ Abdominal aortic aneurysm (AAA) ☐ Carotid artery stenosis (CAS) ☐ Hemodialysis access repair (HAR) ☐ Peripheral arterial disease (PAD) ☐ Other:_____
2. Symptom Status	☐ Symptomatic ☐ Asymptomatic
3. (CEA only) Disease Grading **Refer to Appendix E: Definitions and Acronyms*	☐ Absent ☐ Mild ☐ Moderate ☐ Severe ☐ Unknown
4. (PAD only) Rutherford Classification **Refer to Appendix E: Definitions and Acronyms*	☐ Category 0 ☐ Category 1 ☐ Category 2 ☐ Category 3 ☐ Category 4 ☐ Category 5 ☐ Category 6 ☐ Unknown
5. Target Patch Location	☐ Artery ☐ Vein
If Artery, please select the specific location:	☐ Abdominal aorta ☐ Anterior tibial ☐ Axillary ☐ Brachial ☐ Common carotid ☐ Common iliac ☐ External iliac ☐ Femoral ☐ Internal iliac ☐ Popliteal ☐ Pulmonary ☐ Renal ☐ Subclavian ☐ Superior mesenteric artery ☐ Thoracic aorta ☐ Other:_____
If Vein, please select the specific location:	☐ Anterior tibial ☐ Axillary ☐ Basilic ☐ Cephalic ☐ Common iliac

Medical History eCRF	
	☐ External iliac ☐ External jugular ☐ Femoral ☐ Internal iliac ☐ Internal jugular ☐ Pulmonary ☐ Renal ☐ Subclavian ☐ Superior mesenteric ☐ Other: _____
6. Side of Body	☐ Right ☐ Left ☐ N/A
7. History of Hypertension	☐ None (cutoff point, diastolic pressure usually lower than 90 mm Hg) ☐ Controlled (cutoff point, diastolic pressure usually lower than 90 mm Hg) with single drug ☐ Controlled with two drugs ☐ Requires more than two drugs or is uncontrolled ☐ Unknown
8. History of Hyperlipidemia	☐ Cholesterol (low-density lipoprotein and total) and triglyceride levels within normal limits for age ☐ Mild elevation, readily controllable by diet ☐ Moderate elevation requiring strict dietary control ☐ Moderate elevation but severe enough to require dietary and drug control ☐ Unknown
9. History of Diabetes	☐ None ☐ Adult onset, controlled by diet or oral agents ☐ Adult onset, insulin-controlled ☐ Juvenile onset ☐ Unknown
10. History of Coronary Artery Disease	☐ Yes ☐ No ☐ Unknown
11. History of Congestive Heart Failure **Refer to Appendix E: Definitions and Acronyms*	☐ None ☐ NYHA Class I ☐ NYHA Class II ☐ NYHA Class III ☐ NYHA Class IV ☐ Unknown
12. History of Myocardial Infarction **Refer to Appendix E: Definitions and Acronyms*	☐ None ☐ Recent, < 4 weeks

Medical History eCRF	
	☐ Past, ≥ 4 weeks ☐ Unknown
13. History of Renal Insufficiency	☐ No known renal disease, normal serum creatinine level ☐ Moderately elevated creatinine level, as high as 2.4 mg/dL ☐ Creatinine level, 2.5 to 5.9 mg/dL ☐ Creatinine level greater than 6.0 mg/dL, or on dialysis or with kidney transplant ☐ Unknown
14. History of Stroke	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ ≥4 ☐ Unknown
If ≥1, indicate when the most recent stroke occurred.	_____/_____/_____ Month/Day/Year
15. History of Transient Ischemic Attack (TIAs)	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ ≥4 ☐ Unknown
If ≥1, indicate when the most recent TIA occurred.	_____/_____/_____ Month/Day/Year
16. History of radiation to patch site	☐ Yes ☐ No ☐ Unknown
17. Describe of other significant medical condition	☐ None
18. (AAA/CAS/HAR only) History of Peripheral Arterial Disease	☐ Yes ☐ No ☐ Unknown
19. (CEA only) History of contralateral disease	☐ Normal ☐ < 50% ☐ 50 – 70% ☐ > 70% ☐ Unknown

Surgical History eCRF	
Study Subject ID	
1. History of any cardiovascular surgery	☐ Yes ☐ No ☐ Unknown
If yes, how many prior cardiovascular surgeries	
If yes, how would you classify the surgeries	☐ Cardiac ☐ Vascular (select all that apply)
2. If yes, categorize the surgery (1) **List most recent first*	☐ Open ☐ Endoscopic ☐ Unknown
If yes, describe surgery	
Date of surgery	_____/_____/_____ Month/Day/Year
3. If yes, categorize the surgery (2)	☐ Open ☐ Endoscopic ☐ Unknown
If yes, describe surgery	
Date of surgery	_____/_____/_____ Month/Day/Year ☐ N/A
4. If yes, categorize the surgery (3)	☐ Open ☐ Endoscopic ☐ Unknown
If yes, describe surgery	
Date of surgery	_____/_____/_____ Month/Day/Year ☐ N/A
5. If yes, categorize the surgery (4)	☐ Open ☐ Endoscopic ☐ Unknown
If yes, describe surgery	
Date of surgery	_____/_____/_____ Month/Day/Year ☐ N/A

Social History eCRF	
Study Subject ID	
1. History of Tobacco Use	☐ None or none for last 10 years ☐ None current, by smoked in last 10 years ☐ Current (includes abstinence < 1 year), less than 1 pack/day ☐ Current, ≥ 1 pack/day ☐ Unknown
2. History of Alcohol Use	☐ No ☐ Past ☐ Current ☐ Unknown
If past or current, approximately how many drinks/ per week	☐ Unknown

Imaging Evaluation eCRF	
Study Subject ID	
1. Date Imaging was Performed	_____/_____/_____ Month/Day/Year
2. Indicate Visit Associated with Abstraction of Imaging Data	☐ Visit 1, Pre-op ☐ Visit 2, Peri-Op/Immediately post-op ☐ Visit 3, 1 month post-op ☐ Visit 4, 3 months post-op ☐ Visit 5, 6 months post-op ☐ Unscheduled Visit
3. Select Type of Imaging	☐ Computed Tomography Angiography ☐ Digital Subtraction Angiography ☐ Duplex Ultrasound ☐ Magnetic Resonance Angiography ☐ Transcranial Doppler ☐ Other:_____
4. Reason for Imaging **If AE-related complete AE eCRF*	☐ Scheduled ☐ Adverse Event ☐ Other:_____
5. Evidence of Inflammation/Degeneration in Target Artery/Vein	☐ Yes ☐ No ☐ Unknown
If yes, does this finding affect the patch location?	☐ Yes ☐ No ☐ Unknown
6. Evidence of Stenosis in Target Artery or Vein	☐ Yes ☐ No ☐ Unknown
If yes, indicate degree of stenosis (%)	☐ Unknown
If yes, brief description of technique for determining degree of stenosis	☐ Unknown
If yes, location of stenosis	☐ Unknown
7. Evidence of Calcification in Target Artery/Vein	☐ Absent ☐ Mild ☐ Moderate ☐ Severe ☐ Other:_____ ☐ Unknown
If mild, moderate, severe, or other, does	☐ Yes

Imaging Evaluation eCRF	
the calcification involve the patch area?	☐ No ☐ Unknown
If yes, what percentage of the patch area was affected by calcification (%)?	☐ Unknown
8. (CEA only) Lesion length	☐ No lesion ☐ <15 mm ☐ <15 mm but more than one lesion ☐ >15 mm or if > 2 stents are required ☐ More than one lesion > 15 mm ☐ Unknown
9. (CEA only) Lesion location	☐ No lesion ☐ Lower or mid-neck ☐ Abnormal low below the clavicle ☐ Midneck extending to C2 ☐ Upper neck (C2 or higher/string sign) ☐ Unknown
10. (CEA only) Peak systolic Velocity in Distal Target Common Carotid Artery	☐ Unknown
11. (CEA only) Peak systolic Velocity in Internal Target Carotid Artery	☐ Unknown
12. (CEA only) End Diastolic Velocity in Distal Target Common Carotid Artery	☐ Unknown
13. (CEA only) End Diastolic Velocity in Target Internal Carotid Artery	☐ Unknown
14. (CEA only) Plaque morphology	☐ No plaque ☐ Fibrous plaque/web ☐ Mild calcification ☐ Mixed fibrous/ ulcerative plaques/ thin cap ☐ Multiple large calcification or lipid/ necrotic cores ☐ Unknown
15. (AAA only) Size of AAA (mm)	☐ Unknown
16. Other Significant Imaging Findings	☐ None

Medication eCRF

Study Subject ID:	
Study Visit:	☐ Visit 1, Pre-op ☐ Visit 2, Peri-Op/Immediately post-op ☐ Visit 3, 1 month post-op ☐ Visit 4, 3 months post-op ☐ Visit 5, 6 months post-op ☐ Unscheduled Visit
1. Is the patient currently taking any blood thinners?	☐ Yes ☐ No ☐ Unknown
2. Is the patient currently taking a statin?	☐ Yes ☐ No ☐ Unknown

If yes to either question, please fill out the applicable medication details in the table.

Drug Name	*Indication*	*Dose per Admin.*	*Dose Unit*	*Route of Admin.*	*Dosing Freq.*	*Start Date*	*Stop Date*
1.		☐ Unknown	☐ mg ☐ Other: _____	☐ Oral ☐ Other: _____	☐ Unknown	Month: _____ Day: _____ Year: _____	Month: _____ Day: _____ Year: _____ ☐ Ongoing
2.		☐ Unknown	mg ☐ Other: _____	☐ Oral ☐ Other: _____	☐ Unknown	Month: _____ Day: _____ Year: _____	Month: _____ Day: _____ Year: _____ ☐ Ongoing
3.		☐ Unknown	mg ☐ Other: _____	☐ Oral ☐ Other: _____	☐ Unknown	Month: _____ Day: _____ Year: _____	Month: _____ Day: _____ Year: _____ ☐ Ongoing
4.		☐ Unknown	mg ☐ Other: _____	☐ Oral ☐ Other: _____	☐ Unknown	Month: _____ Day: _____ Year: _____	Month: _____ Day: _____ Year: _____ ☐ Ongoing

Operative Assessment eCRF	
Study Subject ID:	
1. Date of Surgery	_____/_____/_____ Month/Day/Year
2. Implanting Surgeon's Name	
3. Description of Surgical Repair/Reconstruction Involving PhotoFix	
4. Concomitant Procedures Performed	☐ Yes ☐ No
If yes, Description of any Concomitant Surgeries performed	
5. PhotoFix status at conclusion of surgery **If explanted, complete Explant eCRF.*	☐ Implanted ☐ Explanted
6. How many PhotoFix Patches were used in the surgery?	
7. PhotoFix Lot Numbers by Patch Size (Indicated on Packaging)	☐ 0.8 x 8 ☐ 1 x 6 ☐ 1 x 10 ☐ 1 x 14 ☐ 2 x 9 ☐ 4 x 4 ☐ 6 x 8 *Select all that apply
8. Were you able to detect a sidedness to the PhotoFix patch?	☐ Yes ☐ No ☐ Did not check
If yes, which patch side did you implant towards the bloodstream?	☐ Smooth ☐ Rough
9. Perioperative or Post-Operative Adverse Events **If yes, fill out the Adverse Event eCRF.*	☐ Yes ☐ No
If yes, timing of event	☐ Peri-Operative ☐ Post-Operative
10. Length of Implanted Patch (cm)	☐ Unknown
11. Width of Implanted Patch (cm)	☐ Unknown

Follow-Up eCRF	
Study Subject ID	
1. Date of Visit	_____/_____/_____ Month/Day/Year
2. Indicate Visit Number **If Visit 5, fill out End of Study eCRF.*	☐ Visit 3, 1 month post-op ☐ Visit 4, 3 months post-op ☐ Visit 5, 6 months post-op ☐ Unscheduled Visit
3. Indicate Current Subject Status **If withdrawn, fill out End of Study eCRF.*	☐ Active ☐ Withdrawn
4. Were there any post-operative Adverse Events since last study visit? **If yes, fill out the Adverse Event eCRF.*	☐ Yes ☐ No
5. Was patency lost in the target artery/vein since the last study visit? **If yes, fill out the Adverse Event eCRF.*	☐ Yes ☐ No
If yes, indicate the number of instances that patency was lost	
If yes, indicate date(s) patency was lost	_____/_____/_____ (most recent) Month/Day/Year _____/_____/_____ ☐ N/A Month/Day/Year _____/_____/_____ ☐ N/A Month/Day/Year
If yes, indicate reason(s) patency was lost	☐ Aneurysm ☐ Infection ☐ Restenosis ☐ Thrombosis ☐ Other:_____ **Select all that apply*
If yes, was a surgical (open or endovascular) procedure performed to re-establish patency?	☐ Yes ☐ No ☐ Unknown
If yes, was any loss of patency PhotoFix-related?	☐ Definitely ☐ Probably ☐ Possibly ☐ Unrelated
If yes, was patency successfully re-established for the most recent event?	☐ Yes ☐ No ☐ Unknown
6. Did the patient undergo any vascular	☐ Yes

Follow-Up eCRF	
surgery (open or endovascular) since the last study visit? **If yes, fill out the Adverse Event eCRF.*	☐ No ☐ Unknown
If yes, date surgery occurred	_____/_____/_____ Month/Day/Year
If yes, indication for surgery?	☐ Infection ☐ Re-establish Hemodialysis Access Patency ☐ Rupture ☐ Stenosis ☐ Thrombosis ☐ Other:_____ **Select all that apply*
If yes, describe the surgical procedure	
If yes, did the surgery involve PhotoFix or the surrounding patch area?	☐ Yes ☐ No
If yes, was PhotoFix explanted? **If Partially or Completely, fill out Explant eCRF*	☐ No ☐ Partially ☐ Completely
If yes, was the need for surgery related to PhotoFix?	☐ Definitely ☐ Probably ☐ Possibly ☐ Unrelated
7. Has there been evidence of restenosis since the last study visit?	☐ Yes ☐ No ☐ Unknown
If yes, was an imaging evaluation performed **If yes, complete the Imaging Evaluation eCRF*	☐ Yes ☐ No ☐ Unknown
If yes, indicate the degree of restenosis.	☐ Unknown
8. Describe any other significant events which have occurred since the last follow-up visit.	☐ None

Adverse Event eCRF	
Study Subject ID	
1. Date Adverse Event Reported	_____/_____/_____ Month/Day/Year
2. Is this an update to a previously reported event?	☐ Yes ☐ No
3. Start Date	_____/_____/_____ Month/Day/Year
4. Stop Date	____/_____/_____ Month/Day/Year ☐ Ongoing
5. Classify the event as one of the following (if multiple symptoms, classify by most severe)	☐ Amaurosis Fugax ☐ Bleeding event ☐ Cardiac event ☐ Endoleak ☐ Infection ☐ Inflammation/Edema ☐ Pain ☐ Paraparesis ☐ Renal event ☐ Stroke ☐ Symptomatic Carotid Occlusion ☐ Thrombosis ☐ Trauma ☐ Transient Ischemic Attack ☐ Other:_____
(Infection only), was a culture taken?	☐ Yes ☐ No
(Infection only), If yes, what were the reported results?	☐ Inconclusive ☐ Positive (identify organisms):_____ ☐ Negative ☐ Report not available
6. Describe the Event	
7. Consequence of Adverse Event	☐ Surgical Intervention ☐ Hospitalization (New or Prolonged) ☐ Death ☐ Other:_____ ☐ None *Select all that apply

Adverse Event eCRF	
If death is indicated, provide cause of death	☐ Unknown
8. Required Drug Treatment **Update Medication eCRF, as applicable*	☐ Yes ☐ No ☐ Unknown
9. Classify the Adverse Event. **Refer to Protocol Appendix E, Definitions*	☐ Adverse Event (AE) ☐ Unanticipated Adverse Effects (UAE) ☐ Serious Adverse Event (SAE)
If SAE, select at least one of the following	☐ Death ☐ Life Threatening ☐ Other Medically Important Serious Event ☐ Persistent/ Significant Disability ☐ Requires or Prolongs Hospitalization *Select all that apply
10. Is the event related to the subject's vascular surgery?	☐ Yes ☐ No
11. Is the Adverse Event related to PhotoFix?	☐ Definitely ☐ Probably ☐ Possibly ☐ Unrelated
12. Status of Adverse Event	☐ Resolved ☐ Resolved with Sequelae ☐ Not Resolved ☐ Fatal ☐ Unknown
13. Does the Adverse Event Require Study Discontinuation? *If yes, complete the End of Study eCRF*	☐ Yes ☐ No

Explant eCRF	
Study Subject ID	
1. Date of Explant	_____/_____/_____ Month/Day/Year
2. Primary Reason for Explant **Complete Adverse Event eCRF*	☐ Infection ☐ Patch Aneurysm ☐ Patch Deterioration ☐ Rupture ☐ Suture Line Tear ☐ Other:_____
3. Macroscopic evidence of the following:	☐ Calcification ☐ Fibrous Sheathing ☐ Host Tissue Overgrowth ☐ Infection ☐ Inflammation ☐ Thrombosis ☐ Tissue Rejection ☐ Other ☐ Unknown *select all that apply
If any macroscopic findings, provide additional detail.	
4. Was there a pathological analysis of the explanted specimen?	☐ Yes ☐ No ☐ Unknown
If yes, what were the documented pathology results?	
5. Explanting Surgeon	
6. Description of Surgical Procedure	
7. Was the entire PhotoFix patch removed?	☐ Yes ☐ No ☐ Unknown
8. Was peri-operative imaging completed? **If yes, complete the Imaging Evaluation eCRF*	☐ Yes ☐ No ☐ Unknown
9. Were photographs taken of the explanted tissue? **If yes, please e-mail photographs to CryoLife*	☐ Yes ☐ No ☐ Unknown

End of Study eCRF	
Study Subject ID	
1. Date of Discontinuation	_____/_____/_____ Month/Day/Year
2. Indicate Associated Visit	☐ Visit 1, Pre-op ☐ Visit 2, Peri-Op/Immediately post-op ☐ Visit 3, 1 month post-op ☐ Visit 4, 3 months post-op ☐ Visit 5, 6 months post-op ☐ Unscheduled Visit
3. Did the patient complete the study?	☐ Yes ☐ No
If no, Reason for Discontinuation **Complete Adverse Event eCRF, as applicable*	☐ Adverse Event ☐ Death ☐ Did not meet inclusion/ exclusion criteria ☐ Investigator Judgement ☐ Lost-to-Follow-Up ☐ Non-compliance ☐ Pregnancy ☐ Protocol Violation ☐ Termination of Study by Sponsor ☐ Withdrew Consent ☐ Other:_____
If no, provide Details on Discontinuation	☐ No additional details

APPENDIX E: DEFINITIONS AND ACRONYMS

ADVERSE EVENT (AE)
Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a device, whether or not related to the device.

ANIMAL ORIGIN INFECTIOUS AGENT TRANSMISSION
Infection with any organism not commonly found in human beings which can be traced to the animal product by positive culture.

ARRHYTHMIA
An alteration of the heart's rhythm from normal sinus rhythm which requires drug and/or pacemaker therapy.

BLEEDING
Extravascular blood loss requiring volume replacement of surgical interventions

BLEEDING EVENT
Any episode of major internal or external bleeding that causes death, hospitalization, or permanent injury (e.g., vision loss) or requires transfusion. The complication "bleeding event" applies to all patients, whether or not they are taking anticoagulants or antiplatelet drugs, because bleeding events can occur in patients who are not anticoagulated.

CARDIAC ARREST
Permanent or temporary cessation of organized heart function, or precipitous drop in blood pressure sufficiently severe to require cardiopulmonary resuscitation (CPR) or emergency defibrillation.

CAROTID ARTERY STENOSIS (CAS) GRADE
Mild: Amaurosis fugax
Moderate: TIA/minor stroke
Major: Major stroke

COMPLICATION
An undesirable or unexplained clinical event experienced by the patient that results in death, injury, or invasive intervention. Complications may or may not be related to the bypass conduit.

EARLY MORTALITY
Any mortality that occurs within the first 30 days postoperatively.

ELECTRONIC CASE REPORT FORM (eCRF)
An electronic form designed to record protocol required information that is to be reported to the Sponsor on a clinical study patient.

EXPLANT
Removal of the study device for any reason.

FDA
Food and Drug Administration

HEART FAILURE
An event in which the heart fails to meet the circulatory requirements of the body under differing physiological circumstances, and/or a state in which cardiac output is reduced relative to the metabolic demands of the body, assuming the evidence of adequate venous return.

INFECTION
Bacterial or fungal proliferation confirmed by organism culture or systemic or localized reaction.

INFORMED CONSENT
A written document that contains relevant information about the clinical study and that is signed and dated by the patient or the patient's legally acceptable representative.

INSTITUTIONAL REVIEW BOARD (IRB)
An independent body consisting of medical professionals and nonmedical members responsible for reviewing and providing initial and continuing approval of research in human patients and verifying that the safety, integrity, and human rights of patients participating in a particular clinical study are protected.

MORTALITY
Permanent cessation of all vital bodily functions.

MYOCARDIAL INFARCTION
An area of coagulation necrosis resulting from impaired oxygenation of the myocardium. Events that are excluded are those patients who possess normal coronary arteries or if the patient is less than 40 years of age (will be reported as embolism events).

NEW YORK HEART ASSOCATION CLASSIFICATION (NYHA)
Classification system used to categorize a patient's symptoms of heart failure.

NSAID
Nonsteroidal anti-inflammatory drug.

NYHA CLASS I
Patients with cardiac disease but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or angina pain.

NYHA CLASS II
Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

NYHA CLASS III
Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.

NYHA CLASS IV
Patient with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present event at rest. If any physical activity is undertaken, discomfort is increased.

PRINCIPAL INVESTIGATOR
An individual responsible for the conduct of the clinical investigation at a study site. In the event the study is conducted by a team of individuals at a study site, the Principal Investigator is the responsible leader of the team.

REOPERATION
Any operation that repairs, alters, or replaces PhotoFix and/or the surrounding tissue.

RUTHERFORD CLASSIFICATION FOR CHRONIC LIMB ISCHEMIA
Category 0: Asymptomatic—no hemodynamically significant occlusive disease
Category 1: Mild claudication
Category 2: Moderate claudication
Category 3: Severe claudication
Category 4: Ischemic rest pain
Category 5: Minor tissue loss—nonhealing ulcer, focal gangrene with diffuse pedal ischemia
Category 6: Major tissue loss—extending above transmetatarsal level, functional foot no longer salvageable

SERIOUS ADVERSE EVENT (SAE)
A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

SPONSOR
An individual, device company, governmental agency, academic institution, private organization, or organization that takes responsibility for and initiates a clinical investigation.

SUDDEN UNEXPECTED, UNEXPLAINED DEATH
The cause of these deaths is unknown and the relationship to a bypass conduit is also unknown. These deaths should be reported as a separate category of bypass mortality if the cause cannot be determined by clinical data or autopsy.

THIRTY-DAY MORTALITY
Thirty-day Mortality (sometimes termed Operative Mortality) is death within 30 days of operation regardless of the patient's geographic location. Hospital Mortality is any death within

any time interval after operation if the patient is not discharged from the hospital. (Hospital-to-hospital transfer is not considered discharge; transfer to a nursing home or rehabilitation unit is considered hospital discharge unless the patient subsequently dies of complications of the operation.)

UNANTICIPATED ADVERSE EFFECTS (UAEs)

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a product, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the study protocol, or any other unanticipated serious problems associated with a product that relates to the rights, safety, or welfare of a Patient.

APPENDIX F: REFERENCES

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APPENDIX G: PROTOCOL DEVIATION REPORT FORM

integrium Clinical Research

PROTOCOL DEVIATION/WAIVER FORM

Please E-mail this form to: hurley.erin@cryolife.com

To: _____

From: _____

Investigator Name: _____ Phone: _____

Site/Center Number: _____ Fax: _____

Study Name:	PHOTO-V				
Protocol Number:	PHF1801.000-M (04/18)				
Patient Initials:		Patient #:		Visit Date & Visit #:	

All deviations from the protocol that are related to study inclusion or exclusion criteria, conduct of the study, subject management, or subject assessment must be reported using this form.

Investigator's Reason for Deviation:
Please provide a brief summary of the request in the space provided.

Summary: _____

_____

_____

_____

_____

_____

_____

By signing this request you agree that if the deviation occurs the following conditions remain satisfied:

- **The patient's safety is not jeopardized by continuing in the study; and,**
- **In your opinion, the protocol objectives are not compromised.**

PI Signature:		Date:	/ /

Acknowledgement			
CryoLife Signature:		Date:	/ /

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