CLINICAL INVESTIGATIONAL PLAN

ProspeCtive, nOn-randoMized, MulticENter Clinical evaluation of the Edwards Pericardial Aortic & Mitral Bioprostheses (Models 11000A & 11000M) with a new tissue treatment platform (COMMENCE #2012-02)

NCT01757665

March 03, 2021

Protocol Number 2012-02

CLINICAL INVESTIGATIONAL PLAN

Revision J

03 March 2021

ProspeCtive, nOn-randoMized, MulticENter Clinical evaluation of the Edwards Pericardial Aortic & Mitral Bioprostheses (Models 11000A & 11000M) with a new tissue treatment platform (COMMENCE TRIAL)

Trial Sponsor:
Edwards Lifesciences LLC
One Edwards Lifesciences Way
Irvine, CA 92614 USA

1.0 INVESTIGATOR SIGNATURE PAGE

Trial Title:	*ProspeCtive, nOn-randoMized, MulticENter Clinical evaluation of the Edwards Pericardial Aortic & Mitral Bioprostheses(Models 11000A and 11000M) with a new tissue treatment platform (COMMENCE TRIAL)*
Protocol Number:	**2012-02**
Version Number:	**Rev. J**
Date:	**03 March 2021**

I have read this protocol and agree to participate in the clinical investigation of the Model 11000A and Model 11000M sponsored by Edwards Lifesciences LLC. I agree to conduct this investigation according to the requirements of the trial protocol and in accordance with Good Clinical Practice, applicable State and U.S. Federal regulations and conditions imposed by the reviewing Institutional Review Board/Ethics Committee/Research Ethics Board. I agree to supervise all sub-investigators at my site as well as the use of all of the investigational devices at my institution and to ensure appropriate informed consent is obtained from all subjects prior to inclusion in this trial.

INVESTIGATOR NAME	INVESTIGATOR TITLE
INVESTIGATOR SIGNATURE	DATE

2.0 TRIAL CONTACT PERSONNEL

2.1 SPONSOR CONTACT

TRIAL DIRECTOR	TRIAL LEAD / MONITORING

2.2 TRIAL CONTACT

NATIONAL PI	ECHOCARDIOGRAPHY CORE LAB
CLINICAL EVENTS COMMITTEE	**GLYCEROL ASSESSMENT CORE LAB**
DATA MONITORING COMMITTEE	

3.0 PROTOCOL SYNOPSIS

Title:	*ProspeCtive, nOn-randoMized, MulticENter Clinical evaluation of the Edwards Pericardial Aortic & Mitral Bioprostheses(Models 11000A and 11000M) with a new tissue treatment platform (COMMENCE TRIAL)*
Protocol Number	2012-02
Trial Sponsor:	Edwards Lifesciences One Edwards Way Irvine, CA 92614
Trial Device:	Edwards Pericardial Aortic Bioprosthesis, Model 11000A Edwards Pericardial Mitral Bioprosthesis, Model 11000M
Indication for Use:	The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is indicated for patients who require replacement of their native or prosthetic aortic valve. The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is indicated for patients who require replacement of their native or prosthetic mitral valve.
Trial Objective:	The objective of this trial is to confirm that the modifications to tissue processing, valve sterilization, and packaging of the FDA-approved (P860057/S042) Carpentier-Edwards PERIMOUNT Magna Ease Pericardial Aortic Bioprosthesis, Model 3300TFX, which will be designated as the Edwards Pericardial Aortic Bioprosthesis Model 11000A, and the Carpentier-Edwards PERIMOUNT Magna Mitral Ease Pericardial Bioprosthesis, Model 7300TFX, which will be designated as the Edwards Pericardial Mitral Bioprosthesis Model 11000M do not raise any new questions of safety and effectiveness in subjects who require replacement of their native or prosthetic aortic or mitral valve. The only differences between the Model 3300TFX and the Model 11000A and between the Model 7300TFX and the Model 11000M are modifications in tissue processing, valve sterilization, and packaging.
Trial Design:	Multicenter, prospective, double arm trial – Up to seven hundred (700) aortic valve replacement (AVR) subjects and up to one hundred seventy five (175) mitral valve replacement (MVR) subjects at up to forty (40) clinical sites will be enrolled. An enrollment rate of three (3) to four (4) subjects per site per month is anticipated. At least eight (8) centers will implant and follow for at least 1 year,

thirty (30) or more AVR or thirty (30) or more AVR/MVR subjects. Analysis for the aortic arm will be performed when at least three hundred (300) AVR subjects have completed the POD 390 follow-up visit and at least eight hundred (800) AVR patient-years of cumulative follow-up have been reached. Analysis for the mitral arm will be completed when at least three hundred (300) combined aortic and mitral subjects have completed the POD 390 follow-up visit and at least eight hundred (800) AVR and at least one hundred (100) MVR patient-years of cumulative follow-up have been reached. The tests for the trial endpoints were performed and the trial data was submitted to FDA for the PMA approval of the devices evaluated under the aortic and mitral arms. All IDE Subjects (aortic and mitral arms) who are currently enrolled and alive will be followed to 5 years. In an effort to obtain sufficient long-term data, approximately 250 Subjects implanted with the Model 11000A valve at up to 10 sites will be asked to consent for extended follow-up annually through 10 years post-procedure. In addition, approximately 25 Subjects implanted with the Model 11000M valve at select sites will be asked to consent for extended follow-up annually through 10 years post procedure.

Trial Sites:

Participating sites are chosen based on their experience in conducting clinical trials, their surgical experience implanting bioprosthetic valves, as well as their ability to maintain robust subject enrollment and follow-up. The investigational sites will be selected throughout the United States, Canada, Europe and Asia Pacific.

Trial Duration:

Total enrollment period for this trial is estimated to be 1095 days or 3 years. Subject duration in the trial is estimated to be no longer than 1825 days (5 years) or 3650 days (10 years) for those who have consented to continued follow-up. Overall duration of the trial is estimated to be 3833 days or 10.5 years, and will involve at least 800 AVR patient-years and at least 100 MVR patient-years of cumulative follow-up. The trial begins with the enrollment of the first subject and ends after the last subject is exited from the trial after completing the last follow-up visit at approximately postoperative day (POD) 3650, all subjects are fully monitored, all outstanding data queries are resolved and all trial sites are closed to follow-up.

Visit	Visit Window (Days)	Timing from Implant (Day 0)
Screening/Baseline		Day -60 to Day 0

Trial Follow-Up Visits:	Discharge[1]		Prior to Discharge
	POD 30	-5/+10	Day 25 to 40
	POD 105	- 15/+30	Day 90 to 135
	POD 390 (1 yr)	-25/+45	Day 365 to 435
	POD 730 (2 yr)	-25/+45	Day 705 to 775
	POD 1095 (3 yr)	-25/+45	Day 1070 to 1140
	POD 1460 (4 yr)	-25/+45	Day 1435 to 1505
	POD 1825 (5 yr)	-25/+45	Day 1800 to 1870
	POD 2190 (6 yr)*	-55/+75	Day 2135 to 2265
	POD 2555 (7 yr)*	-55/+75	Day 2500 to 2630
	POD 2920 (8 yr)*	-55/+75	Day 2865 to 2995
	POD 3285 (9 yr)*	-55/+75	Day 3230 to 3360
	POD 3650 (10yr)*	-55/+75	Day 3595 to 3725
	[1] Subjects who are not discharged within 10 days post procedure must have an echocardiogram to assess performance of the trial valve. Those subjects will not require an additional echocardiogram at discharge. *Subjects who have consented to continued follow up with the Model 11000A or Model 11000M valve.		

Trial Endpoints:

Primary Safety Endpoint (up to 390 days post-implant):

The primary safety endpoint for the trial is the rate of implanted subjects that experience structural deterioration of the trial valve by the time of the POD 390 follow-up visit. The null hypothesis is that the rate of structural valve deterioration at one year is greater than 1%. The alternative hypothesis is that this rate is less than 1%.

Primary Safety Endpoint (Continued follow-up):

For continued follow-up of Subjects, the primary safety endpoint for the trial is the rate of implanted subjects that experience structural deterioration of the trial valve as determined by a Clinical Events Committee (CEC).

***Secondary Safety Endpoints (Pre-approval)*:**

Safety is established by comparing the occurrence of specific safety endpoints to the objective performance criteria (OPC) reported in Table R.1 in ISO 5840:2009, Annex R.1 as recommended by the FDA in the Draft Guidance involving Heart Valves – Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications (2010).

***Secondary Safety Endpoints (Continued follow-up)*:**

For continued follow-up of Subjects, linearized rates will be used to summarize the following safety endpoints for the late (>30 days) post-operative period.

- Thromboembolism
- Valve thrombosis
- All bleeding/hemorrhage
- Major bleeding/hemorrhage
- All paravalvular leak
- Major paravalvular leak
- Non-structural valve deterioration
- Endocarditis
- All-cause mortality
- Trial valve-related mortality
- Trial valve-related reoperation
- Explant
- Hemolysis

***Effectiveness Endpoints*:**

- Clinically acceptable hemodynamic performance confirmed by core lab evaluation of echocardiography
- New York Heart Association (NYHA) functional class compared to baseline
- Change in Quality of Life questionnaire Short Form 12 version 2 (SF-12v2) from baseline/screening to POD 390

Additional Data in support of analysis:

- Blood Data

Subject Enrollment:

Inclusion Criteria:

Each subject is required to meet all of the following inclusion criteria:

1. Is 18 years or older
2. Provides written informed consent prior to trial procedures
3. Agrees to attend all follow-up assessments for up to 5 years and is willing to comply with specified follow-up evaluations at clinical investigational sites that are participating in the COMMENCE trial and/or obtain the protocol-specified diagnostic tests at centers that are under the same IRB or the same healthcare system
4. Diagnosed with aortic or mitral valve disease requiring valve replacement based on pre- operative evaluation
5. Scheduled to undergo planned aortic or mitral valve replacement with or without concomitant bypass surgery
6. Scheduled to undergo planned aortic valve replacement with or without resection and replacement of the ascending aorta from the sinotubular junction and without the need for circulatory arrest for hemi arch or arch replacement

Exclusion criteria: A subject meeting any of the following criteria shall be excluded:

1. Requires emergency surgery
2. Requires planned multiple valve replacement/ repair (with the exception of mitral valve replacement with tricuspid valve repair)
3. Has prior valve surgery, which included implant of a bioprosthetic valve, mechanical valve, or annuloplasty ring that will remain *in situ*
4. Requires a surgical procedure outside of the cardiac area (e.g. vascular bypass)
5. Requires surgical replacement of the aortic root
6. Has active endocarditis/myocarditis or endocarditis/myocarditis within 3 months to the scheduled aortic or mitral valve replacement surgery
7. Has renal insufficiency as determined by creatinine (S-Cr) level ≥ 2.5 mg/dL or end-stage renal disease requiring chronic dialysis at screening visit
8. Has MRI or CT scan confirmed stroke, cerebrovascular accident (CVA) or transient ischemic attack (TIA) within 6 months (180 days) prior to planned valve surgery
9. Has acute myocardial infarction (MI) within 30 days prior to planned valve surgery
10. Has presence of non-cardiac disease limiting life expectancy to less than 12 months
11. Diagnosed with hypertrophic obstructive cardiomyopathy (HOCM)
12. Diagnosed with abnormal calcium metabolism and hyperparathyroidism
13. Exhibits left ventricular ejection fraction ≤ 20% as validated by diagnostic procedure prior to planned valve surgery
14. Echocardiographic evidence of an intra-cardiac mass, thrombus, or vegetation
15. Hemodynamic or respiratory instability requiring inotropic support, mechanical circulatory support, or mechanical ventilation within 30 days prior to planned valve surgery
16. Documented leukopenia (WBC < 3.5x 10^3/µL), acute anemia (Hgb < 10.0 gm/dL or 6 mmol/L), or thrombocytopenia (platelet count < 50x10^3/µL) accompanied by history of bleeding diathesis or coagulopathy
17. Has prior organ transplant or is currently an organ transplant candidate
18. Current or recent participation (within 6 weeks prior to surgery) in another drug or device trial
19. Was previously implanted with trial device (Model 11000A or Model 11000M)[1]
20. Pregnant (female subject of childbearing potential only), lactating or planning to become pregnant during the duration of participation in trial
21. Currently incarcerated or unable to give voluntary informed consent
22. Documented history of substance (drug or alcohol) abuse within the last 5 years prior to implant
23. Requires concomitant left ventricular assist device (LVAD) placement

4.0 ABBREVIATIONS

ACC	American College of Cardiology
AE	Adverse Event
AHA	American Heart Association
AS	Aortic Stenosis
ASD	Atrial Septal Defect
AVR	Aortic Valve Replacement
CABG	Coronary Artery Bypass Graft
CBC	Complete Blood Count
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
CO/CI	Cardiac Output/Cardiac Index
CRF	Case Report Form
CV	Critical Value
CVA	Cerebrovascular Accident
DIC	Disseminated Intravascular Coagulation
DMC	Data Monitoring Committee
EC	Ethics Committee
eCRF	Electronic Case Report Form
ECG	Electrocardiogram
EDC	Electronic Data Capture
EOA	Effective Orifice Area
FDA	Food and Drug Administration
FMEA	Failure Modes and Effects Analysis
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
HGB	Hemoglobin
HIPAA	Health Insurance Portability & Accountability Act
HCT	Hematocrit
HIT	Heparin Induced Thrombocytopenia
HOCM	Hypertrophic Obstructive Cardiomyopathy
ICF	Informed Consent Form
ICU	Intensive Care Unit
ID	Identification
IDE	Investigational Device Exemption
IE	Infective Endocarditis
IFU	Instructions for Use
INR	International Normalized Ratio
IRB	Institutional Review Board
ISO	International Standardization Organization
LVOT	Left Ventricular Outflow Tract
MI	Myocardial Infarction
MOF	Multi-system Organ Failure
MR	Magnetic Resonance
MVR	Mitral Valve Replacement
NSVD	Nonstructural Valve Dysfunction
NYHA	New York Heart Association
OPC	Objective Performance Criteria
OUS	Outside United States
PFO	Patent Foramen Ovale
PMA	Premarket Approval
PO	Postoperative
POD	Postoperative Day
PT	Prothrombin Time
PTFE	Polytetrafluoroethylene
PTT	Partial Thromboplastin Time
PVL	Paravalvular Leak
QOL	Quality of Life
RBC	Red Blood Cell
REB	Research Ethics Board
RGA	Returned Good Authorization
SAE	Serious Adverse Effect
SAR	Specific Absorption Rate
SAVR	Surgical Aortic Valve Replacement
SMVR	Surgical Mitral Valve Replacement
SF-12	Short Form 12 Health Survey
SVD	Structural Valve Deterioration
TAD	Tissue Annulus Diameter
TEE	Transesophageal Echocardiography
TIA	Transient Ischemic Attack
TTE	Transthoracic Echocardiography
UADE	Unanticipated Adverse Device Effect
WBC	White Blood Cell

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TRIAL PROTOCOL ATTACHMENTS

5.0 TRIAL OVERVIEW

5.1 INTRODUCTION AND BACKGROUND

Valvular heart disease is a life-threatening disease that afflicts millions of people worldwide and leads to approximately 250,000 valve repairs and/or replacements each year. The number of subjects requiring aortic valve replacement (AVR) is increasing due to prolonged life expectancy. Many subjects are asymptomatic until the disease is well advanced and, once diagnosed, have poor prognosis depending on the severity of valve calcification and history of cardiac events[1]. Diseased heart valves can be treated by medication, surgical repair or surgical replacement.

5.1.1 AORTIC AND MITRAL HEART DISEASE

Aortic valvular heart disease includes conditions involving any of the following – obstructions of the aortic heart valve or stenosis; leakage of the aortic valve, known as regurgitation, incompetence, or insufficiency, and combinations of the two, sometimes referred to as mixed disease or combined lesions. Valvular heart disease may be caused by any number of factors, including congenital abnormalities, infection by various micro-organisms, degenerative calcification and rheumatic heart disease. When subjects become symptomatic, angina, syncope, and congestive heart failure (CHF) are the primary clinical signs observed. Studies report that among symptomatic subjects with medically treated moderate-to-severe AS, mortality rates after the onset of symptoms are approximately 25% at one year and 50% at two years. Other studies show that subjects with symptomatic AS have a life expectancy of 2 – 4 years.[2] Neither aortic stenosis nor aortic insufficiency can be effectively treated medically; however, the symptoms of aortic valve disease can be managed medically.

Stenosis of the mitral valve is the narrowing of the valve opening that causes lower blood flow through the valve. In over 99% of stenotic mitral valves, the etiology is rheumatic disease.[3] Other rare causes of mitral stenosis include congenital malformed valves, active infective endocarditis, massive annular calcium, and metabolic or enzymatic abnormalities.[3] Regurgitation of the mitral valve occurs when blood flows back into the valve as the leaflets close or leaks through the leaflets after they are closed. Mitral regurgitation has multiple etiologies including: floppy mitral valves, active or healed infective endocarditis, papillary muscle dysfunction, annular calcium, idiopathic chordae tendineae rupture, rheumatic disease, dilated and hypertrophic cardiomyopathies, endocardial fibrosis, and collagen-vascular disorders (lupus, scleroderma), or Marfan's or Marfan-like disorders. Edward et al reviewed data collected from 1648 patients between January 1990 and December 1999 in northern New England, and noted that mitral valve replacements and repair procedures have substantially increased and indications for these procedures have expanded to also include older and sicker patients with less rheumatic and more degenerative and coronary artery-related mitral valve problems.[4] As the incidence of rheumatic mitral stenosis and regurgitation has decreased, mitral regurgitation caused by degenerative disease of

the mitral apparatus and caused by the left ventricular dysfunction associated with coronary artery disease has become the predominant hemodynamic lesion of the mitral valve.[5]

5.1.2 TREATMENT OF AORTIC AND MITRAL VALVULAR HEART DISEASE

Aortic stenosis and insufficiency can be treated by surgical intervention, including balloon valvuloplasty, valve repair, and valve replacement. Balloon valvuloplasty, a treatment option for aortic stenosis, utilizes a balloon-tipped catheter to stretch open the narrowed valve. Valvuloplasty is predominately used to treat children or adults who are poor surgical candidates. Valve repair techniques include annuloplasty for dilated valve disease, patching leaflet perforations, resected vegetations, or tears, and leaflet extension.[6,7] Aortic valve repair for stenosis does not show good clinical results.[8] Replacement of the aortic valve is indicated for symptomatic subjects and asymptomatic subjects with left ventricular dysfunction.

Diseased mitral valves can be treated by medication, surgical repair and surgical replacement. Repairing the native valve is generally preferred over replacing it. Surgical repair can involve modifying the valve tissue or underlying structures. This procedure can be performed with or without implantation of an annuloplasty ring that provides support to the native valve so that it closes completely and functions normally. If the native valve cannot be repaired, it is replaced by either a mechanical valve (constructed from synthetic material) or a tissue bioprosthetic valve (made primarily from animal tissue including bovine pericardium, or human valves from cadavers.

5.1.3 BIOPROSTHETIC HEART VALVES

Bioprosthetic heart valves are indicated for use in subjects suffering from valvular heart disease. These tissue valves are used particularly in those subjects for whom long-term anticoagulation therapy is contraindicated or who may be difficult to maintain on anticoagulation therapy.

5.2 DEVICE DESCRIPTION

Edwards Pericardial Aortic Bioprosthesis

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A (also referred to as the Model 11000A) is a bioprosthesis comprised of bovine pericardium. It is based on the same design as the Carpentier-Edwards PERIMOUNT Magna Ease Pericardial Aortic Bioprosthesis, Model 3300TFX, which was approved under P860057/S042 on 07 May 2009.

The physical structure and design of the Model 11000A is identical to the Model 3300TFX, except for tissue processing, sterilization and packaging. The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is a trileaflet bioprosthesis comprised of treated bovine pericardium that is mounted on a flexible frame. It is available in sizes 19, 21, 23, 25, 27, and 29 mm. The bioprosthesis is stored in non-aqueous packaging, and does not require rinsing prior to implantation.

The wireform is made of a cobalt-chromium alloy and is covered with a woven polyester fabric. A cobalt-chromium alloy/polyester film laminate band surrounds the base of the wireform frame. A silicone sewing ring that is covered with a porous polytetrafluoroethylene (PTFE) cloth is attached to the wireform frame. The sewing ring has three, equally spaced black silk suture markers at the cusp centers to aid in bioprosthesis orientation and suture placement.

The Model 11000A valve is treated with a new tissue process that builds on Edwards' existing tissue process, ThermaFix (TFX). The new process allows the valve to be stored in non-aqueous packaging and the valve is ethylene oxide sterilized.

Edwards Pericardial Mitral Bioprosthesis

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M is a bioprosthesis comprised of bovine pericardium. It is based on the same design as the Carpentier-Edwards PERIMOUNT Magna Mitral Ease Pericardial Bioprosthesis, Model 7300TFX, which was approved under P860057/S068 on 24 June 2010.

The physical structure and design of the Model 11000M is identical to the Model 7300TFX, except for tissue processing, sterilization and packaging. The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is a trileaflet bioprosthesis comprised of treated bovine pericardium that is mounted on a flexible frame. It is available in sizes 25, 27, 29, 31, and 33 mm. The bioprosthesis is stored in non-aqueous packaging, and does not require rinsing prior to implantation.

The wireform is made of a cobalt-chromium alloy and is covered with a woven polyester fabric. A cobalt chromium alloy/polyester film laminate band surrounds the base of the wireform frame. A waffled silicone sewing ring that is covered with a porous polytetrafluoroethylene (PTFE) cloth is attached to the wireform frame. The sewing ring is scalloped along its anterior portion. Black silk suture markers on the anterior portion facilitate the orientation of the bioprosthesis and help avoid obstruction of the left ventricular outflow tract by a strut. A black silk suture guide line circles the sewing ring.

The Model 11000M valve is treated with a new tissue process that builds on Edwards' existing tissue process, ThermaFix (TFX). The new process allows the valve to be stored in non-aqueous packaging and the valve is ethylene oxide sterilized.

5.2.1 DEVICE INDICATION FOR USE

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is indicated for patients who require replacement of their native or prosthetic aortic valve. The device is contraindicated only if the implanting surgeon decides the anatomy and pathology pose unwarranted risk.

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is indicated for patients who require replacement of their native or prosthetic mitral valve. The device is contraindicated only if the implanting surgeon decides the anatomy and pathology pose unwarranted risk.

5.2.2 DEVICE TRAINING

Training on the Model 11000A and Model 11000M will be per the Instructions for Use (IFUs) provided in ***Attachment B***. The implant technique for the Model 11000A and Model 11000M is the same as other supraannular bioprosthetic valves. The only usage difference in Model 11000A and Model 11000M from other tissue valves is that Models 11000A and 11000M do not require rinsing prior to implantation. If the bioprosthesis is rinsed prior to implantation, the valve must then be kept hydrated with sterile physiological saline irrigation on both sides of the leaflets until the heart is closed.

5.3 REPORT OF PRIOR INVESTIGATIONS

A clinical trial (Protocol Number 2010-03) initiated in Europe in July 2011 is underway to gather data on the Model 11000A. This is a prospective, non-randomized clinical trial of the investigational valve for subjects undergoing aortic valve replacement (AVR). This trial is an observational, confirmatory trial and not powered for statistical analysis. To date, the trial has enrolled one hundred thirty three (133) subjects at two (2) investigational sites in Poland. There are three (3) early deaths, of which two (2) deaths were adjudicated by the CEC as not related to the valve, and one (1) death was adjudicated as valve related.

There are sixteen (16) late deaths, of which three (3) have been adjudicated as valve related. One (1) incident of late study valve related mortality was adjudicated to be due to valve thrombosis, one (1) was adjudicated as to be due to nonspecific/unknown cause, and one (1) valve-related late death was adjudicated to be due to cardiac arrest. As of 7 April 2017, 100% of the eligible subjects completed the discharge, 99.2% completed the 3 month, 97.6% completed the 1 year follow-up, 92.5% completed the 2 year follow-up, 93.8% completed the 3 year follow-up, 92.7% of eligible subjects completed the 4 year follow-up, and 100% completed the 5 year follow up visits. At the time of this interim report there are no occurrences of study valve related bleeding, hemolysis, structural valve deterioration or unanticipated adverse device effects.

Clinical Follow-up

Clinical follow-up endpoints are listed in **Table 1** for the first 133 subjects implanted.

Table 1: Safety endpoints Events (2010-03 Cohort)

Safety Endpoint	Early Events (≤30 POD) N = 133	Late Events (>30 POD) Late pt-yrs = 495.29	
	% (n)	%/pt-yr (m)	95% CL
Mortality	2.3 (3)	3.2 (16)	4.8
Valve-related mortality	0.8 (1)	0.6 (3)	1.4
Thromboembolism	2.3 (3)	0.2 (1)	0.8
Valve thrombosis	0.0 (0)	0.2 (1)	0.8
Major bleeding events	6.8 (9)	0.4 (2)	1.1
Major paravalvular leakage[§]	0.8 (1)	0 (0)	0.5
Endocarditis	0.0 (0)	0.2 (1)	0.8
Structural valve deterioration	0.0 (0)	0 (0)	0.5
Hemolysis	0.0 (0)	0 (0)	0.5
Nonstructural valve dysfunction	0.0 (0)	0.2 (1)	0.8
Reoperation (trial valve)	0.0 (0)	0.2 (1)	0.8
Explant (trial valve)	0.0 (0)	0.2 (1)	0.8

'n' is the number of subjects who experienced the event; 'm' is the number of events observed.
Early event rates are described as simple proportions (n/N); late event rates utilize linearized rates (m/ late pt-yrs).
One-sided upper 95% confidence limit for the linearized rate (CI: Confidence Interval).
[§]Major paravalvular leak is defined as paravalvular leak graded as +3 Moderate or +4 Severe by the Echo Core Lab or any paravalvular leak requiring intervention. Previous report included one late major PVL (+3) and one early minor PVL (+2) in Subject 201003-330 which was reassessed by the Core Lab to be minor late PVL (+2) and no early PVL (0/None).

The investigational valve, Model 11000 is the same design as Model 11000A, and was later renamed as Model 11000A.

6.0 BENEFITS AND RISKS

6.1 BENEFITS

The benefits of the Models 11000A and 11000M are the same as other bioprosthetic valves including improved valvular function, acute alleviation of symptoms related to valve stenosis or insufficiency, and/or improved morbidity and mortality.

The anticipated additional benefits of aortic valve Model 11000A, and mitral valve Model 11000M are to eliminate the need for rinsing the bioprosthesis prior to implantation, less exposure to the risks of glutaraldehyde, and elimination of hazardous waste requiring special disposal.

6.2 RISKS

As with all prosthetic heart valves, serious complications, sometimes leading to death may be associated with the use of tissue valves. Complications due to individual subject reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device. Some or all of the risks listed below could require a reoperation or explant, and/or they may lead to permanent disability or death.

Known/potential risks associated with stented bioprosthetic heart valves include but not limited to:

- Angina
- Bleeding diatheses (coagulopathy) related to anticoagulant therapy
- Cardiac arrhythmias
- Cardiac failure
- Coronary ostial blockage
- Endocarditis
- Hemolysis/Hemolytic anemia
- Hemorrhage
- Immunological response
- Leaflet entrapment (impingement)
- Myocardial infarction
- Nonstructural valve dysfunction
- Paravalvular/Perivalvular leak
- Malfunctions of valve due to distortion at implant, fracture of wireform, physical and or chemical deterioration of valve components
- Patient prosthetic mismatch (PPM)
- Regurgitation/insufficiency
- Stenosis
- Thromboembolism/stroke
- Tissue deterioration including infection, calcification, thickening, perforation, degeneration, suture abrasion, instrument trauma, and or leaflet detachment
- Transient ischemic attack (TIA)
- Valve pannus
- Valve thrombosis

Potential risks associated with aortic valve replacement surgery include but not limited to:

- Allergic reaction
- Annular dissection
- Aortic dissection
- Arterial dissection
- Bleeding, anticoagulant related
- Bleeding, procedural
- Bleeding, post-procedural
- Cardiac arrest
- Cardiogenic shock
- Disseminated intravascular coagulation (DIC)
- Esophageal rupture
- Heart failure
- Hypoxemia
- Infection, local or wound
- Infection, systemic (septicemia)
- Myocardial infarction
- Multi-system organ failure (MOF)
- Pericardial effusion
- Pericardial tamponade
- Pleural effusion
- Pulmonary edema
- Pneumonia
- Renal dysfunction
- Respiratory failure

- Hematoma
- Heparin induced thrombocytopenia (HITs)
- Hypotension
- Hypertension
- Thromboembolism
  - Venous, peripheral or central
  - Arterial, peripheral or central
  - Pulmonary, thrombus or other

Risks associated with Models 11000A and 11000M are anticipated to be the same as those listed above for other aortic or mitral bioprosthetic valves and valve replacement surgery. Based on pre-clinical testing, it is not anticipated that any new risks associated with the Model 11000A and Model 11000M tissue process, sterilization method, or packaging will be observed.

6.3 MINIMIZING SUBJECT RISK

Several safeguards are incorporated into the trial to minimize subject risk. The pre-clinical device testing for the implantable valve was performed in accordance with FDA guidance, ISO 5840:2009 and recognized product standards. All test results met or passed the required specifications supporting reasonable safety for this investigational product.

This clinical trial is conducted under the direction of qualified physicians experienced with cardiac surgery including aortic and mitral valve repair/replacement and the use of investigational devices. All participating investigators and sites are screened and qualified. They must be experienced in conducting clinical research and have adequate personnel to assure compliance to the trial protocol. No special training is required to implant the Models 11000A and 11000M. The Instructions for Use (***Attachment B***) provide detailed instructions on the proper handling and implantation of these investigational valves.

7.0 TRIAL DESIGN

This trial design methodology is based on a one year structural valve deterioration primary endpoint, as discussed in Sections 7.3.1 and 9.0. Based on the results of a pre-clinical assessment and OUS clinical trial, the use of the investigational valve is justified.

7.1 OBJECTIVE

The objective of this trial is to confirm that the modifications to tissue processing, valve sterilization, and packaging of the FDA-approved (P860057/S042) Carpentier-Edwards PERIMOUNT Magna Ease Pericardial Aortic Bioprosthesis, Model 3300TFX, which will be designated as the Edwards Pericardial Aortic Bioprosthesis Model 11000A, and the Carpentier-Edwards PERIMOUNT Magna Mitral Pericardial Bioprosthesis, Model 7300TFX, which will be designated as the Edwards Pericardial Mitral Bioprosthesis Model 11000M do not raise any new questions of safety and effectiveness in subjects who require replacement of their native or prosthetic aortic or mitral valve. The only differences between the Model 3300TFX and Model 11000A, and Model 7300TFX and 11000M are modifications in tissue processing,

valve sterilization, and packaging. The primary safety hypothesis to be accepted or rejected by statistical data is provided in **Statistical Methods Section 9.0**.

7.2 DESIGN

The trial is a multicenter, prospective, double arm trial to be conducted throughout the United States, Canada, Europe and Asia Pacific. It will include subjects with valve stenosis or insufficiency, or stenosis plus insufficiency requiring a planned valve replacement of their native or prosthetic valve. Final analysis for the aortic arm will be performed when at least three hundred (300) AVR subjects have completed the POD 390 follow-up visit, and at least 800 AVR patient-years of cumulative follow-up have been reached. Analysis for the mitral arm will be completed when at least three hundred (300) combined aortic and mitral subjects have completed the POD 390 follow-up visit and at least eight hundred (800) AVR and at least one hundred (100) MVR patient-years of cumulative follow-up have been reached. The tests for the trial endpoints were performed and the trial data was submitted to FDA for the PMA approval of the devices evaluated under the aortic and mitral arms. All IDE Subjects (aortic and mitral arms) who are currently enrolled and alive will be followed to 5 years. In an effort to obtain sufficient long-term data, approximately 250 Subjects implanted with the Model 11000A valve at up to 10 sites will be asked to consent for extended follow-up annually through 10 years post-procedure. In addition, approximately 25 Subjects implanted with the Model 11000M valve at select sites will be asked to consent for extended follow-up annually through 10 years post-procedure.

7.3 ENDPOINTS

All safety and effectiveness data for the Model 11000A and Model 11000M valves will be compared to control data published in articles in the prosthetic heart valve literature.

7.3.1 SAFETY

Primary Safety Endpoint (up to 390 days post-implant):

The primary safety endpoint for the trial is the rate of implanted subjects that experience structural deterioration of the trial valve by the time of the POD 390 follow-up visit. The null hypothesis is that the rate of structural valve deterioration at one year is greater than 1%. The alternative hypothesis is that this rate is less than 1%.

Primary Safety Endpoint (Continued follow-up):

For continued follow-up of Subjects, the primary safety endpoint for the trial is the rate of implanted subjects that experience structural deterioration of the trial valve as determined by a Clinical Events Committee (CEC).

***Secondary Safety Endpoints (Pre-approval)*:**

Safety will be established by comparing the occurrence of specific safety endpoints to the objective performance criteria (OPC) reported in Table R.1 in ISO 5840:2009, Annex R.1 as recommended by the FDA in the Draft Guidance involving Heart Valves – Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications issued January 20, 2010.

***Secondary Safety Endpoints (Continued follow-up)*:**

For continued follow-up of Subjects, linearized rates will be used to summarize the following safety endpoints for the late (>30 days) post-operative period.

- Thromboembolism
- Valve thrombosis
- All bleeding/hemorrhage
- Major bleeding/hemorrhage
- All paravalvular leak
- Major paravalvular leak
- Non-structural valve deterioration
- Endocarditis
- All-cause mortality
- Trial valve-related mortality
- Trial valve-related reoperation
- Explant
- Hemolysis

The Data Monitoring Committee (DMC) will review aggregate safety and hemodynamic data to determine if the trial is being conducted safely and in accordance to the protocol. The DMC will decide if the clinical investigation should be modified, suspended and or stopped.

The Clinical Events Committee (CEC) evaluates the adverse events that are endpoint related as well as those resulting in death. The CEC adjudicates early and late events for their relatedness to the investigational device and/or the surgical procedure.

Adverse event categories are provided in **Section 11.0** and definitions are provided in ***Attachment H –***

Adverse Effect (Codes and Definitions).

7.3.2 EFFECTIVENESS

Effectiveness endpoints include the following:

- Clinically acceptable hemodynamic performance confirmed by echocardiography and core lab evaluation which will include the following parameters:
  - Mean gradient
  - Peak gradient
  - Effective orifice area [EOA]
  - EOA index
  - Performance index
  - Cardiac Output [CO]
  - Cardiac index
  - Valvular regurgitation including paravalvular leak
- New York Heart Association (NYHA) functional class compared to baseline
- Change in Quality of Life assessment – Short Form 12 version 2 (SF-12v2) score from baseline to POD 390.

7.4 ADDITIONAL CLINICAL MEASURES

Additional Data in support of analysis:

- Blood Data
  - White Blood Cell Count
  - Red Blood Cell Count
  - Hemoglobin
  - Hematocrit
  - Platelet Count
  - Plasma free hemoglobin or haptoglobin or serum LDH
  - Coagulation profile (If collected per standard of care dependent on anticoagulation regimen)
  - Serum Glycerol (See Section 10.4.1 for details)

7.5 NUMBER OF SUBJECTS

Up to seven hundred (700) aortic valve replacement (AVR) subjects and up to one hundred seventy five (175) mitral valve replacement (MVR) subjects at up to forty (40) clinical sites will be enrolled. At least eight (8) centers will implant thirty (30) or more AVR or thirty (30) or more AVR/MVR subjects with one year follow-up. An enrollment rate of three (3) to four (4) subjects per site per month is anticipated. Sites with less than ten (10) subjects enrolled will have data combined and reported. Enrollment period completion is anticipated within 1095 days or three (3) years.

7.6 METHODS OF FOLLOW-UP

Following informed consent and determination of eligibility, subjects undergo a pre-operative echocardiogram to document the function of their current valve prior to surgery. Evaluation of the echocardiogram (echo) is performed by a qualified cardiologist/sonographer at the site and over read by an independent core lab. Other baseline exams include physical assessment, recording of pertinent medical history, electrocardiogram (ECG), NYHA classification, Canadian Cardiovascular Society (CCS) Angina classification, quality of life (QOL) assessment, and selected hematological variables.

During the procedure, a transesophageal echo (TEE) and blood collection (if applicable, see Section 10.4.1) will be completed, and a post-operative ECG/rhythm strip will be conducted upon admission to the intensive care unit. In addition, follow-up will occur at or prior to hospital discharge where physical assessment, NYHA classification, CCS Angina classification, ECG, echo and evaluation of selected hematological variables will occur. A post-op echocardiogram must be completed on or prior to post-operative Day 10. At POD 30, a phone follow-up will assess NYHA classification and information on any adverse events that have occurred since discharge. At POD 105 follow-up visit, a physical assessment, NYHA classification, ECG, echocardiogram, and selected hematological variables will be evaluated. The subsequent follow-up visits will be made at POD 390, and annually thereafter up to POD 1825 or 3650. **Table 2** lists the follow-up visit time points and visit windows.

Adverse events and anti-thromboembolic therapy/medications are collected from the time of the index procedure until the subject exits the clinical trial.

Table 2. Visit Follow-Up Schedule

Visit	Visit Window (Days)	Timing from Implant (Day 0)
Screening/Baseline		Day -60 to Day 0
Discharge[1]		Prior to Discharge
POD 30	-5/+10	Day 25 to 40
POD 105	-15/+30	Day 90 to 135
POD 390 (1 yr)	-25/+45	Day 365 to 435
POD 730 (2 yr)	-25/+45	Day 705 to 775
POD 1095 (3 yr)	-25/+45	Day 1070 to 1140
POD 1460 (4 yr)	-25/+45	Day 1435 to 1505
POD 1825 (5 yr)	-25/+45	Day 1800 to 1870
POD 2190 (6 yr)*	-55/+75	Day 2135 to 2265
POD 2555 (7 yr)*	-55/+75	Day 2500 to 2630
POD 2920 (8 yr)*	-55/+75	Day 2865 to 2995
POD 3285 (9 yr)*	-55/+75	Day 3230 to 3360
POD 3650 (10yr)*	-55/+75	Day 3595 to 3725

[1] Subjects who are not discharged within 10 days post procedure must have an echocardiogram to assess performance of the trial valve. Those subjects will not require an additional echocardiogram at discharge.
*Subjects who have consented to continued follow up with the Model 11000A or Model 11000M valve.

8.0 TRIAL POPULATION

8.1 SUBJECT INCLUSION CRITERIA

A subject who meets ***all of the following criteria*** potentially ***may be included*** in the trial:

1. Is 18 years or older
2. Provides written informed consent prior to trial procedures
3. Agrees to attend follow-up assessments for up to 5 years and is willing to comply with specified follow-up evaluations at clinical investigational sites that are participating in the COMMENCE trial and/or obtain the protocol-specified diagnostic tests at centers that are under the same IRB or the same healthcare system
4. Diagnosed with aortic or mitral valve disease requiring valve replacement based on pre- operative evaluation
5. Scheduled to undergo planned aortic or mitral valve replacement with or without concomitant bypass surgery
6. Scheduled to undergo planned aortic valve replacement with or without resection and replacement of the ascending aorta from the sinotubular junction and without the need for circulatory arrest for hemi arch or arch replacement

8.2 SUBJECT EXCLUSION CRITERIA

A subject who meets ***any of the following criteria will not be included*** in the trial:

1. Requires emergency surgery
2. Requires planned multiple valve replacement/repair (with the exception of mitral valve replacement with tricuspid valve repair)
3. Has prior valve surgery, which included implant of a bioprosthetic valve, mechanical valve, or annuloplasty ring that will remain *in situ*

4. Requires a surgical procedure outside of the cardiac area (e.g. vascular bypass)
5. Requires surgical replacement of the aortic root
6. Has active endocarditis/myocarditis or endocarditis/myocarditis within 3 months to the scheduled aortic or mitral valve replacement surgery
7. Has renal insufficiency as determined by creatinine (S-Cr) level ≥ 2.5 mg/dL or end-stage renal disease requiring chronic dialysis at screening visit
8. Has MRI or CT scan confirmed stroke, cerebrovascular accident (CVA) or transient ischemic attack (TIA) within 6 months (180 days) prior to planned valve surgery
9. Has acute myocardial infarction (MI) within 30 days prior to planned valve surgery
10. Has presence of non-cardiac disease limiting life expectancy to less than 12 months
11. Diagnosed with hypertrophic obstructive cardiomyopathy (HOCM)
12. Diagnosed with abnormal calcium metabolism and hyperparathyroidism
13. Exhibits left ventricular ejection fraction ≤ 20% as validated by diagnostic procedure prior to planned valve surgery
14. Echocardiographic evidence of an intra-cardiac mass, thrombus, or vegetation
15. Hemodynamic or respiratory instability requiring inotropic support, mechanical circulatory support, or mechanical ventilation within 30 days prior to planned valve surgery
16. Documented leukopenia (WBC < 3.5x 10^3/µL), acute anemia (Hgb < 10.0 gm/dL or 6 mmol/L), or thrombocytopenia (platelet count < 50x10^3/µL) accompanied by history of bleeding diathesis or coagulopathy
17. Has prior organ transplant or is currently an organ transplant candidate
18. Current or recent participation (within 6 weeks prior to surgery) in another drug or device trial
19. Was previously implanted with investigational device (Model 11000A or Model 11000M)[2]
20. Pregnant (female subject of childbearing potential only), lactating or planning to become pregnant during the duration of participation in trial
21. Currently incarcerated or unable to give voluntary informed consent
22. Documented history of substance (drug or alcohol) abuse within the last 5 years prior to implant
23. Requires concomitant left ventricular assist device (LVAD) placement

[2] Note: Previously implanted means that the index valve replacement procedure was completed. The procedure is complete when the surgeon takes the subject off cardiopulmonary bypass and restarts the heart.

8.3 ENROLLED POPULATION

Subjects will be included in the enrolled population after meeting all the enrollment criteria, signing the informed consent, and after the surgeon assesses the subject's anatomy, sizes the annulus, and determines that the trial valve can be implanted. If the surgeon is unable to complete the implant procedure, the subject is considered "intent to treat" and will be followed for safety (adverse event collection) for 30 days or until any adverse events experienced by subject are resolved. No protocol-specified tests during this period will be required.

Each investigator screens subjects for potential inclusion into the trial. Screening results are used to make a final determination as to subject suitability for enrollment. Early and late results from this trial (i.e., immediate post-operative and up to one year) serve as the basis for determining the safety and effectiveness of the Edwards Pericardial Aortic Bioprosthesis, Model 11000A and the Edwards Pericardial Mitral Bioprosthesis, Model 11000M. Subjects must meet **all** applicable inclusion criteria and **no** pre-operative exclusion criteria at the time of enrollment evaluation in order to participate.

8.4 INDEX VALVE POPULATION

The investigational valve population includes all enrolled subjects that receive and retain the index valve. The analysis of the effectiveness endpoints and of the primary safety endpoint will be based on the investigational valve population.

8.5 SUBJECT AND TRIAL DURATION

Total enrollment period for this trial is estimated to be 1095 days or 3 years. Subject duration in the trial is estimated to be no longer than 1825 days (5 years) or 3650 days (10 years) for those who have consented to continued follow-up. Overall duration of the trial is estimated to be 3833 days or 10.5 years, and will involve at least eight hundred (800) AVR patient-years and at least one hundred (100) mitral valve replacement (MVR) patient-years of follow-up. Trial begins with the enrollment of the first subject and ends after the last subject is exited from the trial after completing the last follow-up visit at approximately POD 3650, all subjects are fully monitored, all outstanding data queries are resolved and all trial sites are closed to follow-up.

8.6 SUBJECT TERMINATION OR WITHDRAWAL

Once enrolled, subjects may discontinue participation at any time by withdrawing informed consent or meeting the requirement for termination. Participation in the trial is entirely voluntary. Subject participation for any patient requiring explant or valve-in-valve (ViV) procedure will be terminated at either 30 days post-explant/ViV (followed for safety only) or when all post-explant/ViV adverse events are resolved (whichever comes last). If the surgeon is unable to complete the implant procedure, those subjects are considered enrolled as "intent to treat" and will be followed for safety (adverse event

collection) for 30 days or until any adverse events experienced by this cohort are resolved and then will be exited from the trial.

9.0 STATISTICAL METHODS

9.1 ANALYSIS POPULATION

The analysis populations will include the enrolled population and the index valve population. The index valve population will include all subjects who meet enrollment criteria, provide written informed consent, those deemed able to implant in the operating room and who receive the index valve. The enrolled population will include the index valve population and the "intent to treat" population[3]. For the enrolled population, the number of patients enrolled per site will be reported. Summaries of baseline and procedural data will be based on the enrolled population. The analysis of mortality and all safety data, including the primary endpoint, shall in general be based on the index valve population; however, the analysis will also be provided using the enrolled cohort. For the investigational valve population, the number of subjects implanted per site will be reported, stratified by implant position and valve size within each position.

9.2 SAMPLE SIZE

The sample size for this study follows the recommendation from the FDA in the Draft Guidance involving Heart Valves – Investigational Device Exemption (IDE) and Premarket (PMA) Applications (2010).

Assuming the Poisson distribution and the true rate being equal to its OPC, and with probabilities of Type I error of 0.05 and Type II error of 0.20, the amount of data necessary to achieve the smallest OPC of 1.2% per patient-year (excluding the OPCs for valve thrombosis, major hemorrhage, and major paravalvular leak, which are all less than 1.2% per patient-year) is 800 patient-years.

9.3 STATISTICAL ANALYSIS

9.3.1 SAFETY ANALYSIS

9.3.1.1 Primary Safety Endpoint (up to 390 days post-implant)

The primary safety endpoint for the trial is the rate of structural deterioration of the study valve at the time of the POD 390 visit. If we let *p* denote the probability that an implanted subject will experience structural valve deterioration by the time of the POD 390 visit, then the null and alternative hypotheses for the primary safety endpoint are:

[3] If the surgeon is unable to complete the implant procedure, those subjects are considered enrolled as "intent to treat" and will be followed for 30 days or until any adverse events experienced by this cohort are resolved and then will be exited from the trial.

$$H_0: p \geq 1\%$$

$$H_a: p < 1\%$$

The statistical test of the null hypothesis for the primary safety endpoint is based on a one-sided, upper 95% confidence interval calculated by the method of Clopper and Pearson[9]:

$$B(0.95; x + 1, n - x)$$

Here x is the number of structural valve deteriorations occurring by the POD 390 visit, n is the number of patients completing the POD 390 visit, and $B(0.95; x + 1, n - x)$ is the 95% upper quantile of the Beta distribution with parameters $x + 1$ and $n - x$. If the confidence interval above is less than 1%, then it will be concluded with 95% confidence that p is less than 1% and the acceptance criterion for the primary safety endpoint will be met. For the purposes of this hypothesis test, both aortic and mitral patients will be combined; however, results for the primary safety endpoint also will be reported separately for each implant position.

Based on a simulation, the power of the confidence interval above to reject the null hypothesis is greater than 80% for the sample size of 300 patients receiving the POD 390 visit. The simulation assumed for the purposes of power calculation a rate of SVD at the POD 390 visit of 0.05%; if a smaller rate is assumed, the power of the statistical test would of course be higher. The code for this simulation has been provided to FDA and is included in ***Attachment O***.

9.3.1.2 PRIMARY SAFETY ENDPOINT (CONTINUED FOLLOW-UP):

For continued follow-up of Subjects, the primary safety endpoint for the trial is the rate of implanted subjects that experience structural deterioration of the trial valve as determined by a Clinical Events Committee (CEC). The linearized rate will be calculated as the number of late events divided by the total number of late-subject years. These results will be reported for both implant positions combined and separately for each position.

9.3.1.3 Secondary Safety Endpoints (Pre-approval)

The secondary safety endpoints listed in **Section 7.3.1** will be analyzed using the enrolled population. Early adverse events within 30 days of procedure will be reported as the number of events divided by the number of enrolled subjects. Linearized rates will be used to summarize adverse events for the late (>30 days) post-operative period. The linearized rates will be calculated as the number of late events divided by the total number of late-subject years. In addition, a one-sided upper 95% confidence limit will be calculated for the linearized rate.

The hypotheses for the secondary safety endpoints are:

$$H_0 : p \geq 2 \times OPC \quad vs. \quad H_A : p < 2 \times OPC$$

where *p* is the complication rate for a given valve-related event. If the one-sided sided upper 95% confidence limit for *p* for a given secondary endpoint is less than $2 \times OPC$ then the trial will be considered a success with regards to that secondary endpoint. These hypotheses will be tested based on the combined aortic and mitral populations; however the results will also be reported separately for each implant position.

Percentages for the early events and linearized rates for the late events also will be calculated for all other complications observed in the trial, including structural deterioration. These results will be reported for both implant positions combined and separately for each position.

Actuarial rates based on the method of Kaplan - Meier will be calculated for SVD and for each of the safety events in Section 7.3.1 at each of the follow-up time points; the number of subjects at risk for the event will be reported at each of these intervals. These results will be reported for both implant positions combined and separately for each position.

9.3.1.4 SECONDARY SAFETY ENDPOINTS (CONTINUED FOLLOW-UP):

For continued follow-up of Subjects, percentages for the early events and linearized rates for the late events also will be calculated for all other complications observed in the trial, including structural deterioration.

Actuarial rates based on the method of Kaplan - Meier will be calculated for SVD and for each of the safety events in Section 7.3.1 at each of the follow-up time points; the number of subjects at risk for the event will be reported at each of these intervals. These results will be reported for both implant positions combined and separately for each position.

9.3.2 EFFECTIVENESS ANALYSIS

The following effectiveness endpoints will be analyzed using the investigational valve population. The analysis for valve performance will be performed separately for each implant position, and the analyses for NYHA Class and Quality of Life will be performed for both implant positions combined, separately for each position, and for isolated mitral valve replacement and mitral valve replacement with concomitant tricuspid valve repair.

9.3.2.1 VALVE PERFORMANCE

The following parameters will be summarized at baseline and at each follow-up visit for all subjects in the investigational valve population

- Peak pressure gradient
- Mean pressure gradient
- Effective orifice area
- Valvular regurgitation
- Effective orifice area index
- Performance index
- Cardiac output
- Cardiac index

Valvular regurgitation will be summarized by the number and percentage of subjects in each level of regurgitation. All other parameters will be summarized by N, mean, and standard deviation, and a 95% confidence interval. These summaries will be stratified by valve size.

9.3.2.2 NYHA CLASS

A comparison of preoperative and postoperative NYHA functional class (presented as the percentage of subjects in each class at baseline, at each follow-up time-point, and as the percentage of subjects at each follow-up time-point who improved, worsened, or did not change in class) will be presented. This comparison will be based on the investigational valve population. Additionally, a cross-tabulation of baseline vs. POD 390 NYHA will be presented for all subjects in the investigational valve population with both baseline and POD 390 NYHA data.

9.3.2.3 QUALITY OF LIFE

The N, mean and standard deviation for the SF-12 physical and mental health summary measures (PCS-12 and MCS-12, respectively) will be calculated for baseline and POD 390. In addition, the N and mean for the change from baseline to POD 390 in PCS-12 and MCS-12 will be presented with a 95% confidence interval. These summaries will be based on the investigational valve population.

9.4 ADDITIONAL MEASURES

9.4.1.1 BLOOD DATA

For all measured blood parameters, individual results will be compared to documented normal ranges. The Investigator will determine for each parameter that is out-of-range whether the value is not clinically significant and summary statistics will be provided.

Summary statistics (N, mean, and standard deviation) will be calculated preoperatively and post-operatively. In addition, the percentage of patient within the normal range preoperatively and post-operatively will be calculated. The percentage of patients within the normal range post-operatively will be reported separately for patients within and without the normal range preoperatively and for all patients combined.

Analyses of blood data will be performed for both implant positions combined and separately for each position.

9.5 POOLABILITY

Subject baseline risk will be statistically compared between the regions (US, Canada, Europe and Asia Pacific) and among centers for the implanted population. Chi-square tests will be used to compare categorical risk factors while analysis of variance will be used to compare continuous risk factors. Comparisons will be based on the following demographic and pre-operative variables: age, sex, etiology, pre-operative NYHA, and concomitant CABG procedures, and any other baseline risk factors as deemed appropriate.

One-year Kaplan Meier estimates for the implanted population will be compared between the regions (US, Canada, Europe and Asia Pacific) and among sites for the following events: thromboembolism, valve thrombosis, major bleeding/ hemorrhage, all paravalvular leak, endocarditis, explant, and death. Estimates will be compared via a log-rank test. The primary safety endpoint will not be compared between regions or sites as it is expected that no structural valve deteriorations will be observed within the first year at any site or within any region.

9.6 ANALYSIS OF COVARIATES

A hazard regression analysis will be performed to test for the effect of gender, age at implant, pre-operative NYHA functional classification, previous valve surgery, concomitant coronary artery bypass surgery, implant position, and implant size on survival. This analysis will be performed by using a Cox proportional hazards model and will be based on the implanted population. Additionally, one-year Kaplan Meier estimates for each of the adverse events listed in the **Safety Endpoints Section 7.3.1** will be compared between the genders via a log-rank test.

Finally, the effect of gender on each of the following effectiveness endpoints at POD 390 (1 year) will be investigated with a linear regression model: peak gradient, mean gradient, effective orifice area (EOA) index. These linear regression models will be adjusted by BSA (to adjust for the effect of body size), implant position, and by valve size. The effect of gender on all valvular regurgitation at POD 390 (1 year) will be investigated via an ordinal logistic regression; this model also will be adjusted by BSA, implant position, and by valve size. All analyses will be based on the implanted population.

9.7 MISSING DATA

All statistical tests on the effectiveness endpoints will be performed using only those subjects with available data required for endpoint analysis. No missing value imputation will be performed.

9.8 FOLLOW-UP AND COMPLIANCE DATA

The number of valve population subjects followed to 390 days post-implant will be reported stratified by site and valve size; follow-up duration information, including mean follow-up, standard deviation and range of follow-up, and cumulative follow-up in subject-years will be reported for the valve population.

Subject compliance will be calculated and reported as the following four percentages: the number of subjects a) having completed follow-up visits; b) with NYHA functional classification data; c) with echocardiographic data; and d) with clinical laboratory results at each follow-up time-point, divided by the total number of implanted subjects available (i.e., who have not died or had their valve explanted) and eligible (i.e., who have reached the given time-point) for follow-up at that particular time-point. Compliance will be reported for each follow-up visit and will be based on the investigational valve population.

10.0 TRIAL PROCEDURES

10.1 SUBJECT SCREENING

All subjects diagnosed with aortic or mitral stenosis, insufficiency or stenosis-insufficiency requiring valve replacement as assessed by cardiac surgeons participating in this clinical trial, should be screened for eligibility. All subjects who may meet eligibility requirements will be asked to participate.

A "Screening Log" is provided to the investigational sites to maintain a cumulative log of all screened subjects. For subjects who are ineligible for participation in the clinical investigation, a reason supporting the disqualification of the subject must be entered on the Screening Log. Sites are not required to enter data into the EDC system for any preoperative or intraoperative screen failures. Any subject deemed ineligible due to active or recent endocarditis/myocarditis, recent myocardial infarction, pregnancy or lactation, or participation in another clinical investigation may be re-screened later. Re-screened subjects must be re-entered on the Screening Log.

10.2 INFORMED CONSENT

Written informed consent, in accordance with applicable international standards and trial center regulations, shall be obtained from each subject, prior to the trial procedures. The investigator retains a copy of the signed informed consent document in each subject's record, and provides a copy to the subject.

The Investigator must obtain the written informed consent of all subjects, and must not allow any subject to participate in the investigation prior to obtaining governing institutional review board (IRB), research ethics board (REB) approval, or Ethics Committee (EC) approval. Before starting the trial, the investigator provides trial Sponsor with a copy of the sample Informed Consent document approved by the IRB, REB, or EC with documented evidence that the IRB, REB, or EC approved the protocol and the informed consent.

Attachment C provides an example of a consent form submitted to each IRB, REB, or EC. The example form contains the minimal consent language content that must be incorporated into the Informed

Consent document. Other elements may be added or minor language changes may be made for clarity by the investigator or by the IRB/REB/EC, but substantial content may not be deleted.

10.3 BASELINE ASSESSMENT

After a written informed consent is obtained from the subject, the following baseline data is obtained as noted in **Table 3** below. This data includes physical assessment, demographic and medical history, 12-lead electrocardiogram (ECG), transthoracic echocardiogram (TTE) or transesophageal echocardiogram (TEE) per protocol, blood studies, an assessment of NYHA Functional Classification, CCS Angina Classification, an assessment of quality of life (QoL), and coagulation profile (via INR or PTT). Test results conducted within **60 days** before planned valve surgery may be used for this trial if all values are available and are no significant changes in the subject's condition would invalidate the test results.

Table 3. Baseline Assessment

Clinical/Physical Assessment		Blood Studies	Echocardiography
Date of Assessment	Anti-thromboembolic Therapy (medications)	Blood Draw Date	Date of Exam
Date of Birth		White Blood Cell Count	
Sex/Gender		Red Blood Cell Count	
Height	Cardiovascular Risk Factors	Hemoglobin	***REFER TO ECHO MANUAL***
Weight	Cardiovascular Conditions	Hematocrit	
Heart Rate	Previous Procedures / Interventions	Platelet Count	
Blood Pressure		Plasma Free Hemoglobin or haptoglobin or serum LDH	
Cardiac Rhythm (12-lead ECG)	Non-Cardiovascular Conditions	Serum Creatinine	
NYHA Classification	Pregnancy Test	Coagulation Profile	
CCS Angina Classification			
Quality of Life (SF-12)			

10.4 VALVE REPLACEMENT PROCEDURE

All procedures are performed in an operating room, or a surgical suite having cardiac surgery and anesthesia services. The surgical approach used is at the discretion of the Investigator's routine surgical practice. At the time of valve replacement, transesophageal echocardiography (TEE) is recommended to assess the subject's anatomy. After performing the aortotomy, the native valve and surrounding anatomy will be examined for compatibility with the investigational device.

Note: The Edwards Pericardial Bioprostheses, Models 11000A and 11000M do not require rinsing prior to implant. ***Note:*** If the valve is rinsed prior to implant, it must be kept hydrated with sterile physiological solution throughout the remainder of the surgical procedure. Rinsing every 1-2 minutes is recommended. ***Caution:*** Contact of the leaflet tissue with any articles or sources of particulate matter should be avoided.

Transesophageal echocardiography (TEE) should be performed within 1 hour after the bioprosthesis is implanted (from cross-clamp removal) to assess placement and bioprosthesis function. The echocardiography requirements may be found in ***Attachment E***. A post-operative ECG or rhythm strip should also be performed upon arrival to the intensive care unit (ICU).

10.4.1 SERUM GLYCEROL ANALYSIS

In order to obtain serum glycerol levels in a minimum of 100 subjects, the first 15 subjects enrolled at each of 8 sites will be evaluated. Two (2) blood samples for this assay will be collected from each of these subjects, one (1) pre-operatively (post-heparinization) and one (1) between 60 and 120 minutes after the heart has been restarted. The time that each sample is drawn will be recorded, as will the time the heart was restarted.

Samples will be appropriately labeled, frozen and shipped to the Glycerol Assessment Core Laboratory following the instructions provided in the Serum Glycerol Sample Collection Manual (***Attachment F***). Any subject who becomes an intra-operative screen failure will be replaced with next consecutively enrolled subject until up to 15 subject samples are achieved at each of the 8 sites.

Procedural information, findings, results and device identification information to be recorded are identified in **Table 4.**

Table 4. Procedural Information

General Information	Clinical Information	Device Information
Date of Admission Date of Procedure Implanting Surgeon Type of Operation	Etiology Diagnosis for Replacement Valve Implant/ Valve Position Sizing Condition of the Native Valve Concomitant Procedures Intra-operative Adverse Events Post-operative Cardiac Rhythm upon arrival to ICU *Blood collection for Glycerol Analysis (See Section 10.4.1) **REFER TO SERUM GLYCEROL SAMPLE COLLECTION MANUAL**	Valve Size and Serial Number Valve Performance Post-operative TEE (within 1 hour) **REFER TO ECHO MANUAL**

10.5 POST INDEX VALVE IMPLANT

At the discretion of the investigator, bioprosthetic heart valve recipients should be maintained on anticoagulant therapy (except when contraindicated) during the initial healing stage after implant, in accordance with the ACC/AHA 2006 Guidelines for the Management of Subjects with Valvular Heart Disease. However, the appropriate anticoagulation therapy must be determined by the physician on an individual basis.

10.6 DISCHARGE

The medical information and clinical evaluation of trial subjects prior to discharge is identified in **Table 5.** Subjects not discharged within 10 days post procedure, must have an echocardiogram to assess placement and performance of the index valve. This echocardiogram is required to complete the evaluation of short-term valve function. Those subjects will not require an additional echocardiogram at

discharge.

Table 5. Discharge Information

Clinical/Physical Assessment	Blood Studies	Echocardiography (TTE)
Date of Discharge Weight Heart Rate Blood Pressure Cardiac Rhythm (12-lead ECG) Anti-thromboembolic Therapy (medications) Adverse Events	Blood Draw Date White Blood Cell Count Red Blood Cell Count Hemoglobin Hematocrit Platelet Count Plasma Free Hemoglobin or haptoglobin or serum LDH Coagulation Profile	Date of Exam **REFER TO ECHO MANUAL**

10.7 POST DISCHARGE FOLLOW-UP ASSESSMENTS

A summary of the tests and measurements to be conducted at screening, operatively, prior to discharge, and during follow-up are illustrated in the Clinical Trial Scheme in ***Attachment A.***

A telephone follow-up visit is conducted at POD 30 (-5/+10 days) to document anti-thromboembolic therapy (medications), adverse events and determine NYHA and CCS Angina functional classification.

Post-procedure clinical evaluation is performed on all trial subjects at the investigational site. Information to be recorded at scheduled visits is further detailed in **Table 6.**

During each postoperative follow-up visit, the investigator(s) will determine the subject's availability for future follow-up visits. If any subject needs to be seen at a time other than a regularly scheduled follow-up visit, and the data will be recorded as an interim visit, and any applicable data pertinent to the visit will be collected. Coagulation profile is only required if collected per standard of care dependent on anticoagulation regimen (i.e. non-Vitamin K oral anticoagulants (NOAC's) do not require monitoring of coagulation profile).

Table 6. Follow-Up Information at all Post-Discharge Visits

Clinical/Physical Assessment	Blood Studies	Echocardiography (TTE)
Date of Discharge Weight Heart Rate Blood Pressure Cardiac Rhythm (12-lead ECG) NYHA Classification CCS Angina Classification Quality of Life (SF-12)* Anti-thromboembolic Therapy (medications) Adverse Events	Blood Draw Date White Blood Cell Count Red Blood Cell Count Hemoglobin Hematocrit Platelet Count Plasma Free Hemoglobin or haptoglobin or serum LDH Coagulation Profile**	Date of Exam **REFER TO ECHO MANUAL**

*Conducted only at the POD 390 visit **Only required if collected per standard of care dependent on anticoagulation regimen

All efforts should be taken by the Investigator and the research staff to encourage subjects to return for required follow-up visits. If a subject cannot return for follow-up visits, all attempts will be made to collect the protocol-specified data from outside hospitals or clinics. For echocardiography exams performed outside of the trial site, a copy of the Core Laboratory Procedure Manual is provided in ***Attachment E*** to ensure compliance with the echocardiography requirements.

10.8 MISSED FOLLOW-UP

The Investigator(s) will make every attempt to follow the subjects. All subjects will be encouraged by the Investigator(s) to report any address or telephone number changes to the trial site. They are informed of the importance of returning for scheduled follow-up visits even if they are not having any medical issues.

If a subject cannot be reached for a follow-up visit, the Investigator will document on the CRF, the efforts undertaken to contact the subject or the subject's primary health care provider. These efforts should include three (3) attempts of telephone contact at separate dates and times, and a registered letter sent before the end of the follow-up window (telephone attempts may include a family member if available). If a subject cannot be reached for a follow-up visit, or misses a scheduled visit, the visit will be recorded as a missed visit on the date of last attempted contact. Subjects who miss a visit will not be considered withdrawn. At the next visit interval, the Investigator and/or designee will make three (3) attempts of telephone contact at separate dates and times, and a registered letter sent before the end of the follow-up window (telephone attempts may include a family member if available). Subjects who miss two (2) sequential follow-up visits will be considered lost to follow-up at the second missed visit and exempt from further trial follow-up. After the subject is terminated from the trial, the Investigator will attempt to determine if the subject is alive, including searching national mortality registries as permitted by local laws.

Trial Subjects exit the trial when no additional follow-up visits, procedures, or data collection are required. A subject is exited from the trial in the following instances:

- Fails enrollment criteria after written consent
- Is Lost-to-follow-up (LTFU)
- Voluntarily withdraws from the trial
- Death
- Explant or valve-in-valve (ViV) intervention (after 30 days for safety endpoints only; or after adverse events from explant/ViV are resolved, whichever comes later)
- Does not retain trial valve after attempt to implant (after 30 days for safety endpoints only; or after adverse events from explant are resolved, whichever comes later)
- Completes last trial follow-up visit (at POD 1825 or POD 3650 for Continued Follow-Up Subjects)
- Investigator withdraws the subject from the trial

10.9 DEVICE REMOVAL OR EXPLANT

Index valve 'removal' is the excision of the investigational valve, before implant of the investigational valve is complete, i.e., the subject does not leave the OR with the investigational valve. If the surgeon is unable to satisfactorily position or sew in the index valve, it will be removed and returned to the trial Sponsor who will provide a return valve kit. If the subject leaves the OR with the investigational valve in place, the valve will be considered implanted and if removal is required from this point forward, it will be considered an explant.

In the event a valve is explanted/ requires a valve-in-valve intervention, a copy of the procedure report must be provided to the trial Sponsor. Information on the cause of explant and its relationship to the valve will be provided by the investigator(s). Explanted valves must be returned to the trial Sponsor for analysis. Return kits for devices will be provided by the trial Sponsor.

11.0 ADVERSE EVENTS

11.1 REPORTING

Adverse event information is reported throughout the clinical investigation. Adverse events are followed until they are adequately resolved. *A list of potential adverse events, which may result from the trial procedure, are included in the* Risk Section 6.2*, the Instructions for Use (IFU) in* ***Attachment C,*** *and further defined in* ***Attachment G***.

11.1.1 UNANTICIPATED ADVERSE DEVICE EFFECT

An ***unanticipated adverse device effect (UADE)*** is any serious adverse effect on health or safety or any life threatening problem or death caused by or associated with the device, if that effect, problem, or death was not previously identified in nature, severity, degree of incidence in this Investigational Plan. Additionally, an unanticipated adverse event includes any other unanticipated serious problem associated with the device that relates to the rights, safety, or welfare of subjects.

Investigator(s) are required to submit to the reviewing IRB/REB/EC and the trial Sponsor a report of any ***unanticipated adverse device effect (UADE)*** occurring during this investigation as soon as possible, but in no event later than two (2) business days after the investigator(s) first learns of the effect (21CFR 812.150(a)(l)). The trial Sponsor must immediately conduct an evaluation of an UADE, and must report the results of the evaluation to FDA, all reviewing IRB/REB/ECs, and participating investigators within ten (10) business days after the trial Sponsor first receives notice of the effect (21CFR 812.46(b), 812.150(b)(l)).

If it is determined that an UADE occurred, the trial Sponsor will notify the Data Monitoring Committee (DMC) within five (5) business days after the trial Sponsor or its designee first receives notice of the event. If the trial Sponsor and/or the DMC determines an event or event rate presents an unreasonable risk to a

subject, all investigations or parts of investigations presenting that risk are terminated, as soon as possible. Termination of the investigation shall occur no later than five (5) working days after the trial Sponsor makes this determination and no later than fifteen (15) days after trial Sponsor or its designee first receives notice of the event.

11.1.2 ADVERSE DEVICE EFFECTS

An adverse event is any undesirable experience associated with the use of a medical product in a patient. The event is serious and should be reported to FDA (and other relevant regulatory agencies) when the subject outcome is/led to:

- Death
- Life-threatening
- Hospitalization or prolonged hospitalization
- Disability or permanent damage
- Congenital Anomaly or birth defect
- Intervention to prevent permanent impairment or damage
- Other serious or important medical events – medical or surgical intervention to prevent one of the above outcomes

.

Investigational sites report all applicable serious adverse events in accordance with the reviewing IRB/REB/EC committee's requirements.

Trial Sponsor or its designee determines reportability of applicable adverse events according to its responsibilities for European vigilance reporting.

11.2 NOTIFICATION OF UADE AND/OR SERIOUS DEVICE RELATED ADVERSE EFFECTS

Notification of UADE and serious device related adverse effects should be done via email to HVTClinicalResearch@edwards.com or faxed to 949-809-5610.

11.3 DEATH AND EXPLANTS

In the event of subject death, every effort should be made to obtain a copy of the autopsy report and/or death summary. Information on the cause of death and its relationship to the device used in this clinical trial will be determined by the investigator(s). Copies of an autopsy report, if available, and/or a death summary are to be sent to the trial Sponsor.

If a device is explanted during autopsy, the device should be returned to the trial Sponsor for analysis. Return kits for devices will be provided by the trial Sponsor.

11.4 DATA MONITORING COMMITTEE

The trial Sponsor will appoint a Data Monitoring Committee (DMC) composed of two or more independent physicians including a cardiothoracic surgeon and a cardiologist, and a statistician. Members of the DMC will not have scientific, financial, or other conflict of interest related to the trial Sponsor or the Investigators. Curricula Vitae for the DMC members are maintained by the trial Sponsor, and are available for regulatory review. These individuals may not participate in this trial as investigators, and may not hold significant material, financial or other interests, which create a potential conflict with respect to this role. DMC members must sign a non-conflict-of-interest statement in this regard.

The primary purpose of the DMC is to ensure a consistent, independent review of events and their clinical significance using standardized criteria and definitions. The DMC will be tasked with identifying any issues such as higher than expected AE and/or death rates, UADEs or hemodynamic performance that is substantially worse than expected, to determine if the trial should be stopped, suspended, or modified at any time. The DMC will establish guideline criteria for recommending trial termination.

The DMC will meet at least yearly or more often as determined by the Chairperson and possibly on an *ad hoc* basis to evaluate trial progress and results during the enrollment phase. The Chairperson of the DMC will be informed of all UADEs within five (5) business days of these events being reported to the trial Sponsor or its designee. This requirement, in addition to the guideline criteria for recommending trial termination, will be incorporated into the DMC charter.

11.5 CLINICAL EVENTS COMMITTEE

The Clinical Events Committee (CEC) evaluates adverse events that are endpoint related. The CEC adjudicates events for their relatedness to the investigational device and/or the surgical procedure. The CEC will be composed of physicians familiar with the treatment of valvular heart disease and cardiac surgery and who are not participating in the investigational trial.

The trial Sponsor will provide the CEC completed case report forms and any relevant source documentation/subject information as provided by the clinical site investigators. The trial Sponsor will insure that all information is de-identified before presenting to the committee. The CEC documents its findings or rulings on each event. All meeting minutes and supporting documentation are maintained by the CEC administrator with a copy provided to the trial Sponsor.

12.0 TRIAL AND DATA MANAGEMENT

12.1 TRIAL CORE LABS

12.1.1 ECHOCARDIOGRAPHY CORE LAB

The Echocardiography Core Lab is responsible for independently evaluating echocardiograms submitted preoperatively and postoperatively by trial sites, and for reporting of hemodynamic and other valvular function results. The purpose of the Echocardiography Core Lab is to ensure unbiased, timely and consistent analysis of the diagnostic data, and for evaluating changes in subject status over the course of the trial based on serial echocardiographic studies conducted on the same subject.

Personnel at the Echocardiography Core Lab must demonstrate appropriate training and experience for analyzing Doppler Echocardiography data. The trial Sponsor or its designee periodically will audit the Echocardiography Core Lab. Echocardiograms will be sent directly from the investigational sites to the Echocardiography Core Lab. The Echocardiography Core Lab reviews the Doppler echocardiograms upon receipt, and promptly notifies the site and the trial Sponsor if the quality of the echocardiograph is insufficient for analysis. The Echocardiography Core Lab will enter the data into the eCRF. See ***Attachment E*** for the Core Laboratory Procedure Manual.

12.1.2 GLYCEROL ASSESSMENT CORE LAB

The Glycerol Assessment Core Lab is responsible for independently analyzing all blood samples collected for measurement of serum glycerol. The purpose is to ensure unbiased, timely and consistent analysis of the data. See ***Attachment F*** for the Serum Glycerol Sample Collection Manual.

12.2 DEVICE ACCOUNTABILITY

An initial set of Edwards Pericardial Bioprostheses Models 11000A and/or 11000M, is shipped to the clinical site once the following conditions are met: the site obtained regulatory approval (Institutional Review Board, Ethics Committee approval or Research Ethics Board), a signed Clinical Trial Agreement is in place, and the Site Initiation Visit, including Principal Investigator training, is complete. Additional devices are sent to the clinical site as devices are used or as needed.

12.2.1 INVENTORY AND ACCOUNTABILITY RECORDS

A Device Accountability Log is maintained by the Investigator noting all investigational devices received for use during this clinical trial. The log is kept with the documents for the clinical trial and is available for review during trial Sponsor monitoring visits.

All device shipments include inventory and shipment records (packing slip). The Principal Investigator or designee will take inventory of the product, note the condition of the device, and attest to accuracy of the valve shipment by signing the packing slip. Both the investigational site and the trial Sponsor retain copies of the packing slips and the Device Accountability Log.

12.2.2 DEVICE STORAGE

The device inventory is to be stored in a locked, controlled, cool, dry and clean area. This storage area shall be accessible only to the Principal Investigator(s), Co-Investigator(s) or approved designee(s). Only cardiac surgeons identified in the Clinical Trial Agreement and/or on the Delegation of Authority form on file may implant the investigational device.

12.2.3 DEVICE RETURN

The Principal Investigator(s) is notified in writing upon termination of the clinical trial. All unused devices in original package and/or those in opened packages will be returned upon receipt of this notice as described in the IFU. The Investigator's copy of the Device Accountability Log must document any unused devices that are returned. The trial Sponsor will provide shipping instructions.

12.3 PROTOCOL DEVIATIONS

A protocol deviation is defined as an event where the Investigator or trial personnel did not conduct the trial according to the clinical protocol or the Clinical Trial Agreement.

Deviations shall be reported to the trial Sponsor regardless of whether medically justifiable or taken to protect the subject in an emergency. Subject specific deviations and non-subject specific deviations, (e.g. unauthorized use of a trial device outside the trial, unauthorized use of a trial device by a physician who is not listed in the Clinical Trial Agreement, etc.) will be reported in writing. Investigators will adhere to procedures for reporting trial deviations to the IRB/EC/REB in accordance with their specific reporting policies and procedures.

For reporting purposes, deviations are classified as major or minor:

- **Major deviations** – will be reported to the trial Sponsor within 48 hours but no later than 3 business days of awareness of the major deviation and document on the appropriate case report form provided; and to the IRB/REB/EC per their guidelines
  - Any deviation from subject inclusion and exclusion criteria
  - Any deviation from subject informed consent procedures
  - Unauthorized use of an investigational device outside the trial
  - Unauthorized use of an investigational device by a physician who is not listed in the Clinical Trial Agreement

- **Minor deviations** – will be reported to the trial Sponsor in writing on the appropriate form provided
  - Deviation from a protocol requirement such as incomplete/inadequate testing procedures;
  - Follow-up performed outside specified time windows in the protocol

  NOTE: Information that is not essential to the trial endpoints is not considered a deviation if absent.

12.4 TRIAL SITE INITIATION AND MONITORING PLAN

12.4.1 SITE INITIATION AND TRAINING

Site staff will be trained and experienced to perform their delegated tasks. Training may be in person, webinar, read and review, or other methods as deemed appropriate.

Training is documented on a "Training Log". A "Delegation of Authority Form" is completed at each site designating which individuals are allowed to perform specific clinical trial related tasks. The delegated tasks will determine what the training requirements are for each member of the trial support staff.

New research staff members may be trained by previously trained personnel on the Delegation of Authority Form.

12.4.2 MONITORING

Written procedures have been established by the trial Sponsor for monitoring clinical investigations, to assure the quality of the trial and to assure that each person involved in the monitoring process carries out his or her duties. Standardized written procedures, sufficiently detailed to cover the general aspects of clinical investigations, will be used as a basic monitoring plan and will be supplemented by more specific / additional procedures specific to this clinical investigation.

A pre-trial monitoring visit or meeting will be conducted to ensure that the Investigator clearly understands and accepts the obligations incurred in undertaking the clinical investigation as listed in **Table 7** (Regulations and Guidelines), and that the facilities are acceptable. Periodic monitoring visits will be conducted with adequate frequency to ensure that the Investigator's obligations as set forth in 21 CFR Part 56 and 21 CFR Part 812 are being fulfilled and that the facilities continue to be acceptable.

The trial Sponsor will assign a monitor to oversee the progress of the clinical investigation at each investigational center. The monitor will remain in close contact with each investigational center throughout the duration of the investigation to provide any needed materials, (i.e., investigation forms) and answer any questions. The monitor will be responsible for verifying that the subject signed the consent, reviewing all data recorded on the eCRFs, and visiting each investigational center periodically to observe trial progress and compliance with clinical protocol and regulations applicable to this clinical investigation. Additionally, the monitor will provide assurance that complete records are being maintained, appropriate timely reports are made to the trial Sponsor and IRB/REB/EC, device inventory is controlled, and that the Investigator is carrying out all agreed upon activities. Any personnel changes must be reported to the monitor immediately and a training program must be scheduled and documented. A trial termination monitoring visit will be conducted at the completion of the clinical trial to ensure that all data are properly documented and reported.

Site Termination: If a clinical monitor becomes aware that an Investigator is not complying with the signed Investigator's Agreement, the Investigational Plan, the requirements of applicable health authority regulations, or any conditions of approval imposed by the reviewing IRB/REB/EC or health authority, trial Sponsor will immediately either secure compliance or terminate the Investigator's participation in the trial. The final action will be taken with the goal of assuring the rights, safety and welfare of the patients.

12.5 DOCUMENTATION REQUIREMENTS

12.5.1 SOURCE DOCUMENTS

Clinical regulations require that Investigators maintain information in the clinical trial subject's medical records that corroborate data collected on the eCRF. Some examples of critical information to be maintained for review by the regulatory inspectors and trial Sponsor monitors are:

- Medical history and physical condition of the clinical trial subject before involvement in the clinical trial sufficient to verify protocol entry criteria
- Dated and signed notes in the subject's medical record on the day of entry into the clinical trial
- Dated and signed notes, laboratory records, and test reports, from each clinical subject visit with reference to the eCRF for further information, if appropriate (for specific results of procedures and exams).
- Notations on abnormal lab results, adverse events reported and their resolution
- Notes regarding concomitant anticoagulant/antithrombotic medications taken during the clinical trial
- Subject's condition upon completion of or withdrawal from the clinical trial.

To protect subject confidentiality, the subject's name must not appear anywhere on the imaging media sent to trial Sponsor e.g. for reporting serious adverse device effects (SADE), or prepared for evaluation by the core lab. Each page should be identified with the subject's unique trial ID number. All other subject identifiers (i.e. medical record number, personal number) are to be obscured. Original copies of all data must be kept at the site.

Site monitoring will include 100% primary source verification of events contributing to the safety and effectiveness endpoints and unanticipated adverse device effects (UADE).

12.5.2 TRIAL DOCUMENTS

The trial Sponsor will provide pre-printed forms to each trial site for documentation of:

- Investigator and site training to the protocol (Training Log)
- Authorized trial site personnel (Delegation of Authority)

- Subject consent and screening (Screening and Enrollment Log)
- Monitoring visit tracking (Site Visit Log)
- Investigational Device Accountability (Investigational Device Accountability Log)

The site visit is recorded on the appropriate site visit report. All tasks and action items noted during the visit should be documented with detailed findings and comments provided as appropriate. The monitor provides a visit follow-up letter to the investigator and other appropriate trial staff briefly summarizing the visit and specifically addressing any outstanding issues and/or action items from the visit, any incidents of noncompliance with the protocol or applicable regulations noted during the visit, and any necessary corrective actions.

During the course of the clinical trial, all correspondence (letters, records of telephone calls, emails and faxes) regarding the trial must be maintained in the regulatory binder provided by the trial Sponsor. This binder must be made available for monitoring visits and audits.

12.6 DATA COLLECTION

All required data for this trial are to be collected with standardized Case Report Forms (CRF) for individual subjects; the eCRF outline is included in ***Attachment D***. Electronic CRF (eCRF) will be utilized for this trial. Each eCRF must be signed electronically by the Principal Investigator listed in the Clinical Trial Agreement and Delegation of Authority Log. If for any reason an eCRF is unavailable and/or inaccessible, a paper CRF will be provided by the trial Sponsor to be completed, signed by the Principal Investigator or designee and submitted to the trial Sponsor.

Case Report Form Instructions will be provided to assist the Investigator(s) and appropriate trial staff with the completion of each required eCRF.

The Sponsor's data management group is responsible for database development, validation, control and management of input from each monitored CRF, issuance and resolution of queries, database maintenance, and statistical support. Data Management personnel will employ a full-featured relational Oracle database application (or equivalent) on a central server that is 21 CFR Part 11 compliant. The application provides the capability of data collection remotely through the Internet so the participating site personnel may log on to the system securely and enter the data. Other data management programming and/or data analyses will be done in the database system through the trial Sponsor's internal network.

12.7 DATA AND DOCUMENT RETENTION

Trial-related correspondence, subject records, consent forms, records of device implant, and source document worksheets are to be maintained on file by the trial site. The trial Sponsor requires that it be notified in writing if the Principal Investigator wishes to relinquish ownership of the data and information

so that mutually agreed upon arrangements can be made for transfer of ownership to a qualified entity. Per FDA regulation 21 CFR 812.140, records of each subject's participation in the trial must be maintained for a period of two (2) years after trial closure and submission of the final report to the IRB/REB/EC.

12.8 TRIAL PROTOCOL AMENDMENTS

Changes in the protocol are made only by written amendment agreed upon by the trial Sponsor, the applicable regulatory agency, including the United States Food and Drug Administration, and if pertinent, the IRB/REB/EC. As appropriate, the trial Sponsor will submit changes in the protocol to the applicable regulatory agencies, including the United States Food and Drug Administration and investigators to obtain IRB/REB/EC re-approval. A report of withdrawal of IRB, REB or EC approval must be submitted to the trial Sponsor **within five (5) business days**. Any revisions to the protocol, including the Informed Consent Form and the Case Report Forms, other than very minor revisions must be approved by trial Sponsor, the IRB/EC/REB and the FDA and/or other regulatory agencies.

12.9 TRIAL COMPLETION

The principal investigator will be notified in writing upon termination/conclusion of the clinical trial. The trial Sponsor retains the right to suspend or terminate this clinical trial at any time.

A final clinical report shall be compiled once data collection is complete. Such reports include all information required and outlined in this protocol. The final report will be provided to regulatory agencies and/or institutional review boards/independent ethics committees and other regulatory agencies as per applicable laws. The final clinical report will be filed in the clinical trial master file.

12.10 FUTURE PLANS

No changes are planned at this time.

13.0 STATEMENTS OF COMPLIANCE, CONFIDENTIALITY AND RESPONSIBILITIES

13.1 GOOD CLINICAL PRACTICE STATEMENT

This trial will be conducted in compliance with all applicable US Federal regulations pertaining to investigational devices including but not limited to: 21 CFR Part 50, Part 54, Part 56, Part 812, Good Clinical Practice (GCP) standards, and Health and Insurance Portability and Accountability Act (HIPAA). The protocol and supporting documents for this trial will be reviewed and approved by an appropriately constituted IRB, REB or EC prior to trial initiation. All reviews and approvals will be in accordance with Good Clinical Practice (GCP) and all other applicable standards, regulations (local and national), guidelines and institutional policies.

13.1.1 PROTECTION OF SUBJECT CONFIDENTIALITY

Subject confidentiality will be maintained in accordance with GCP, the HIPAA and all other applicable standards, regulations (local and national), guidelines and institutional policies.

13.2 REGULATIONS AND GUIDELINES

The regulations listed in **Table 7** must be observed to comply with the trial Sponsor's policy for conduct of clinical studies; they represent good clinical practice. It is the responsibility of the investigator(s) to comply with the requirements set forth in their country specific regulations.

Table 7. Regulations and Guidelines

Country or Region	Regulation / Guideline
US	- Investigational Device Exemption (IDE), 21 CFR Part 812 - Institutional Review Board (IRB), 21 CFR Part 56 - Protection of Human Subjects, 21 CFR Part 50 - Financial Disclosure, 21 CFR part 54 - Draft Guidance for Industry and FDA Staff - Heart Valves – Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications, January 20, 2010
Europe	- 93/42/EEC European Medical Device Directive (MDD) - ISO 14155:2011 (Clinical Investigation of Medical Devices for Human Subjects) - ISO 5840:2009 (Cardiovascular implants-Cardiac valve prostheses) - Declaration of Helsinki (2008)
Canada	- Canadian Medical Device Regulations (CMDR) - Canadian Investigational Testing Authorization as defined in the Medical Devices Regulation, May 1998
Asia Pacific	- Regional requirements will be added in an Appendix as required.

13.3 INVESTIGATOR RESPONSIBILITIES

The trial Investigator(s) will adhere to the trial protocol, Good Clinical Practice, HIPAA, and compliance with applicable government and institutional regulations. The trial Investigator(s) is responsible for obtaining proper regulatory approvals, and reporting to regulatory authorities per all applicable regulations. ***Attachment J*** provides a comprehensive list of Investigator(s) responsibilities.

13.4 SPONSOR RESPONSIBILITIES

The trial Sponsor will adhere to the trial protocol, Good Clinical Practice, HIPAA, and compliance with applicable government and institutional regulations. The trial Sponsor is responsible for obtaining proper regulatory approvals, and reporting to regulatory authorities per all applicable regulations. ***Attachment J*** provides a comprehensive list of trial Sponsor responsibilities.

14.0 PUBLICATIONS

Edwards Lifesciences, as the trial Sponsor of record, has a proprietary interest in this trial. Authorship and manuscript composition will reflect cooperation between multiple investigators and sites, core laboratories, and Edwards Lifesciences. Authorship will be established prior to writing of the manuscript. No individual publications will be allowed prior to the completion of the final report for this trial and as agreed in writing by Edwards Lifesciences.

15.0 REFERENCES

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ATTACHMENT A – CLINICAL TRIAL SCHEME

CLINICAL TRIAL SCHEME

Schedule of Tests:	**Baseline**	**Procedure (Day 0)**	**Discharge**	**30 Days (Phone)**	**105 Days**	**390 Days**	**730-3650 Days[7]**
Signed Informed Consent	X						
Physical Exam[1]	X		X		X	X	X
Medical History[2]	X						
Blood Labs[3]	X	X	X		X	X	X
ECG	X	X	X		X	X	X
Echocardiogram[4]	X	X	X		X	X	X
NYHA Class/ CCS Angina Class	X			X	X	X	X
QOL Questionnaire (SF-12 v2)	X					X	
Coagulation Profile[5]	X		X		X	X	X
Anti-thromboembolic Therapy & Medications	X		X	X	X	X	X
Pregnancy Test[6]	X						
Adverse Events		X	X	X	X	X	X

[1] Physical exam: height, weight and vital signs [BP, HR].

[2] Includes cardiovascular & non-cardiovascular conditions, prior cardiac interventions and surgeries.

[3] Blood labs: CBC [RBC, WBC, Hgb, HCT, PLT], plasma free hemoglobin or haptoglobin or serum LDH; Serum creatinine is required only at baseline.

Serum glycerol is only required at the procedure interval (See Section 10.4.1).

[4] TTE will be the standard echocardiography assessment for the aortic or mitral valve. TEE intra-operatively or within 1 hour (from cross clamp removal) to confirm placement of the device and confirm initial function of the valve.

[5] Coagulation profile will be determined for subjects on anticoagulant therapy only, where coagulation profile is collected per standard of care. Non-Vitamin K oral anticoagulants (NOACs) that do not require monitoring of coagulation profile, for example, will not require collection/reporting of coagulation profile.

[6] Applicable only to females of child bearing age.

[7] All IDE subjects to be followed to POD 1825 (5 yrs). All Subjects implanted with the Model 11000A or Model 11000M valve who have consented to continued follow-up will be followed annually through 10 years post-procedure.

ATTACHMENT B – INSTRUCTIONS FOR USE

Edwards Lifesciences

DIRECTORY

English

Edwards Pericardial Aortic Bioprosthesis, Model 11000A

Instructions for use

CAUTION: Investigational device. Limited by Federal (United States) law to investigational use.

CAUTION: Investigational device. Exclusively for Clinical Investigations.

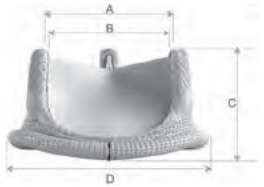
Caution: Investigational Device. Limited to Investigational Use. To be used by Qualified Investigators (Physicians).

1. Device and Accessories Description

1.1 Device Description

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is a trileaflet bioprosthesis comprised of treated bovine pericardium that is mounted on a flexible frame. It is available in sizes 19, 21, 23, 25, 27, and 29 mm (Table 1). The bioprosthesis is stored in non-aqueous packaging, and does not require rinsing prior to implantation.

Table 1. Nominal Dimensions



Size	19 mm	21 mm	23 mm	25 mm	27 mm	29 mm
A. Tissue Annulus Diameter (Stent Diameter, mm)	19	21	23	25	27	29
B. Internal Diameter (Stent ID, mm)	18	20	22	24	26	28
C. Profile Height (mm)	13	14	15	16	17	18
D. External Sewing Ring Diameter (mm)	24	26	28	30	32	34
Geometric Orifice Area (mm^2)	235	289	354	420	499	570

The wireform is made of a cobalt-chromium alloy and is covered with a woven polyester fabric. A cobalt-chromium alloy/polyester film laminate band surrounds the base of the wireform frame.

A silicone sewing ring that is covered with a porous polytetrafluoroethylene (PTFE) cloth is attached to the wireform frame. The sewing ring has three, equally spaced black silk suture markers at the cusp centers to aid in bioprosthesis orientation and suture placement.

A holder is attached to the bioprosthesis by means of sutures to facilitate handling and suturing the bioprosthesis during implantation. The holder is easily detached by the surgeon. (See **10.4 Device Implantation**)

1.2 Accessories Description

Sizers and Tray

The use of a sizing instrument facilitates selection of the correct size bioprosthesis for implantation. The translucent Model 1133 sizers permit direct observation of their fit within the annulus. Each sizer consists of a handle with a different sizing configuration at each end (Figure 1a). On one side of the handle is a cylindrical end with an integrated lip that reflects the bioprosthesis sewing ring geometry (Figure 1b). On the other side of the handle is a bioprosthesis replica end that reflects the bioprosthesis sewing ring geometry as well as the height and location of the stent posts (Figure 1c). A sizer is available for each size of the Model 11000A bioprosthesis (19, 21, 23, 25, 27, and 29 mm). The complete set of sizers is housed in a tray, Model TRAY1133, which can be reused and resterilized.

Figure 1a. Aortic Sizer

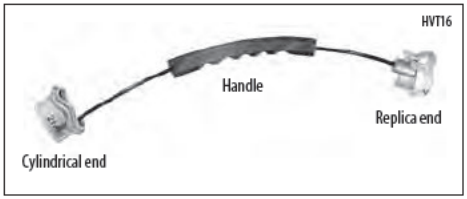


Figure 1b. Cylindrical End

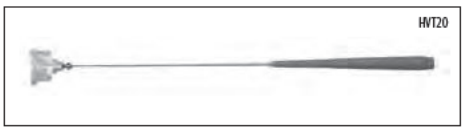
Figure 1c. Replica End

Bioprosthesis Holder and Handle

The handle/holder assembly consists of two components: an integral disposable part that is physically mounted to the bioprosthesis by the manufacturer and a malleable handle (reusable Model 1111 or disposable Model 1126 for single use) that is attached to the holder at the time of surgery (Figures 2a and 2b).

Figure 2a. Model 1111 Handle

Figure 2b. Model 1126 Handle



2. Indications for Use

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is indicated for patients who require replacement of their native or prosthetic aortic valve.

3. Contraindications

Do not use the bioprosthesis if the surgeon believes use is contrary to the best interests of the patient. The decision for or against use of this bioprosthesis remains with the surgeon who must evaluate all the various risks involved, including the anatomy and pathology observed at the time of surgery.

4. Warnings

FOR SINGLE USE ONLY. This device is designed, intended, and distributed for single use only. Do not resterilize or reuse this device. There are no data to support the sterility, non-pyrogenicity, and functionality of the device after sterile reprocessing.

DO NOT FREEZE OR EXPOSE THE BIOPROSTHESIS TO EXTREME HEAT. Exposure of the bioprosthesis to extreme temperatures will render the device unfit for use.

DO NOT USE the bioprosthesis:

- **If the foil pouch, sealed trays, or lids are opened, damaged, or stained**
- **If the expiration date has elapsed, or**
- **If it is dropped, damaged, or mishandled in any way. Should a bioprosthesis be damaged during insertion, do not attempt repair.**

DO NOT EXPOSE the bioprosthesis to any solutions, chemicals, antibiotics, etc., except for sterile physiological saline solution. Irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.

DO NOT GRASP the leaflet tissue of the bioprosthesis with instruments or cause any damage to the bioprosthesis. Even the most minor leaflet tissue perforation may enlarge in time to produce significant impairment of bioprosthesis function.

DO NOT OVERSIZE. Oversizing may cause bioprosthesis damage or localized mechanical stresses, which may in turn injure the heart or result in leaflet tissue failure, stent distortion and regurgitation.

As with any implanted medical device, there is a potential for patient immunological response. Some components of the model 11000A are a metal alloy that contains cobalt, chromium, nickel, molybdenum, manganese, carbon, beryllium and iron. Care should be exercised in patients with hypersensitivities to these materials. This device was manufactured without latex, but may have been produced in a latex-containing environment.

5. Adverse Events

5.1 Observed Adverse Events

As with all prosthetic heart valves, serious adverse events, sometimes leading to death, may be associated with the use of tissue valves. In addition, adverse events due to individual patient reaction to an implanted device or to physical or chemical changes to the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device.

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A is similar in design to the Carpentier-Edwards PERIMOUNT Magna Ease Pericardial Bioprostheses, Model 3300TFX.

Adverse events associated with the use of Carpentier-Edwards PERIMOUNT pericardial bioprostheses compiled from the literature and from reports received through the product surveillance system in accordance with the United States (Federal) regulations establishing Good Manufacturing Practices, section 820.198, include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulation therapy, and malfunctions of the valve due to distortion at implant, fracture of the wireform, or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, degeneration, suture abrasion, instrument trauma, and leaflet detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia, fever, arrhythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarction.

Note: Based on reports in the literature on tissue valves (Refs. 6, 7, 8, 9 & 10), there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies (Ref. 11) show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes a potential relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult (Ref. 13). When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. There are no clinical data demonstrating increased resistance of the Edwards Pericardial Aortic Bioprosthesis Model 11000A to calcification as compared to other commercially available bioprostheses.

5.2 Potential Adverse Events

Adverse events potentially associated with the use of bioprosthetic heart valves include:

- Angina
- Bleeding diatheses (coagulopathy) related to anticoagulant therapy
- Cardiac arrhythmias
- Coronary ostial blockage
- Endocarditis
- Heart failure
- Hemolysis
- Hemolytic anemia
- Hemorrhage
- Local and/or systemic infection
- Myocardial infarction
- Patient prosthetic mismatch (PPM)
- Prosthesis leaflet entrapment (Impingement)
- Prosthesis nonstructural dysfunction
- Prosthesis pannus
- Prosthesis perivalvular leak
- Prosthesis regurgitation
- Prosthesis structural deterioration
- Prosthesis thrombosis
- Stroke
- Thromboembolism
- Transient ischemic attack (TIA)

It is possible that these complications may lead to:

- Reoperation
- Explantation
- Permanent disability
- Death

6. Clinical Studies

Pre-Approval Patient Cohort

Clinical data, available on 719 patients requiring isolated aortic valve replacement (AVR) with the model 2700 Carpentier-Edwards PERIMOUNT pericardial bioprosthesis with mean follow-up of 3.9 years, indicate overall actuarial survival rate at 6 years of 73.7% ± 2.0%. Clinical data, available on 70 patients requiring double valve replacement (DVR) with mean follow-up of 3.7 years, indicate overall actuarial survival rate at 6 years of 67.2% ± 6.5%. These pre-approval patient cohort data were collected from the period between August 1981 to January 1989.

In the isolated AVR population, there were a total of 455 (63.3%) males and 264 (36.7%) females with a mean age at implant (± standard deviation) of 64 (± 12.4) years and a range of 18 to 90 years. The indications for valve replacement were stenosis (63.4%), regurgitation (16.3%), mixed disease (15.3%) and previous prosthetic aortic valve dysfunction (5.0%).

In the DVR population, there were a total of 24 (34.3%) males and 46 (65.7%) females with a mean age (± standard deviation) of 62.9 (± 12.7) years and a range of 31 to 94 years. The indications for valve replacement were stenosis (45.7%), regurgitation (25.7%), mixed disease (21.4%) and previous prosthetic aortic valve dysfunction (7.4%).

The follow-up methods included hospital visits, office visits and contact by telephone or letter with either the patient, the patient's family or local doctor.

Table 2 summarizes the operative and postoperative complication rates for the isolated AVR and DVR populations. The operative rates are based on 719 patients for the isolated AVR population and on 70 patients for the DVR population. The postoperative rates are based on 2767.9 and 255.8 years of follow-up occurring > 30 days after implant for the isolated AVR and DVR populations, respectively.

Table 3 presents, by valve size, the postoperative echocardiography results of patients in this study population.

Information on preoperative and postoperative NYHA Functional Class was gathered for the isolated AVR population. The NYHA Functional Class was not reported in 220 patients (171 patients expired and 49 patients not available). Of the 499 patients with reported preoperative and postoperative NYHA Functional Class at the last available follow up, 10 patients, (2.0%) got worse, 59 patients (11.8%) remained the same and 430 patients (86.2%) improved.

Table 4 presents data comparing preoperative NYHA Functional Class to postoperative NYHA Functional Class at the last available follow up.

Post-Approval Patient Cohort

Edwards has followed a post-approval cohort of 267 patients with isolated valve replacements (AVR) (model 2700) from four centers of the original clinical trial for the Carpentier-Edwards PERIMOUNT pericardial bioprosthesis since November 1981. The population is comprised of 171 (64%) males and 96 (36%) females. The mean age (± standard deviation) of these patients at the time of implant was 64.9 ± 11.8 years and ranged from 21 to 86 years. A total of 2,407 patient years of data were available for analysis (2,386 late patient years). Mean follow-up was 9.0 ± 5.5 years, with a maximum of 20.3 years. A total of 189 deaths occurred between 1981 and 1994. Forty-eight (25.3%) of the 189 deaths were determined to be valve-related. The follow-up methods used at each clinic included hospital visits, office visits, and contact by telephone or letter with either the patient, the patient's family, or local doctor.

Table 5 summarizes the freedom from complication rates at 20 years. Patient status as of the last follow-up interval included 189 expired (70.8%), 10 alive (3.8%), 46 explanted (17.2%), and 22 lost to follow-up (8.2%).

There were a total of 48 valve-related expirations in this patient population; 1 valve-related expiration occurred in the operative period and consisted of bleeding. Twenty-eight postoperative valve-related expirations included 5 due to thromboembolism, 4 due to endocarditis/sepsis, 3 due to structural valve deterioration and 1 due to bleeding. There were 15 other expirations that were considered to be valve-related because of lack of information or because the expiration was classified as valve-related by the investigator. The actuarial freedom from valve-related expiration was 67.9 ± 6.6% at 20 years. Nineteen additional expirations were due to either unknown causes or sudden death and might have been valve related. These deaths were conservatively classified as valve related; accordingly, the resulting actuarial freedom from valve-related expiration was 55.4 ± 6.4% at 20 years.

Improvement in NYHA functional classification also was demonstrated postoperatively. As of the latest follow-up evaluation, 108 patients (44.8%) were in NYHA Functional Class I.

These data were compiled from a multi-center clinical trial conducted by Edwards Lifesciences. For additional information on this trial, please contact Edwards Lifesciences LLC, Heart Valve Therapy Marketing Department, One Edwards Way, Irvine, CA 92614-5686.

Confirmatory Study

From August 2003 through January 2004, 60 patients requiring aortic valve replacement (AVR) were implanted with the Carpentier-Edwards PERIMOUNT Magna aortic bioprosthesis, model 3000, from five institutions (two European and three Canadian). Shortly thereafter, the clinical protocol was amended to allow implantation with the Carpentier-Edwards PERIMOUNT Magna aortic bioprosthesis, model 3000TFX, and to add three US institutions. Subsequently, 193 additional patients were implanted with the model 3000TFX from December 2004 through December 2006. The model 3000TFX differs from the model 3000 in that the model 3000TFX is treated with the ThermaFix process.

In the model 3000TFX population, there were a total of 116 males (60.1%) and 77 females (39.9%) with a mean age at implant of 72.0 (± 8.59 SD) years and an age range from 26 to 89 years. The main indication for valve replacement was stenosis (78.2%) followed by mixed disease (14.5%), and regurgitation (7.3%).

In the combined models 3000 and 3000TFX population, there were a total of 150 males (59.3%) and 103 females (40.7%) with a mean age at implant of 72.2 (± 8.31 SD) years and an age range from 26 to 89 years. Again the major indication for valve replacement was stenosis (77.5%), mixed disease (15.4%), and regurgitation (7.1%).

Patients were evaluated preoperatively, intraoperatively, at discharge, at 3 to 6 months, at 1 year, and annually thereafter. The cumulative follow-up for the model 3000TFX was 167 patient-years, with a mean follow-up of 0.9 years (SD = 0.42, range = 0.0 to 2.1 years); and the cumulative follow-up for both models 3000 and 3000TFX combined was 232 patient-years with a mean follow-up of 0.9 years (SD = 0.42, range = 0.0 to 2.1 years).

Table 6 summarizes early (≤ 30 days) and late postoperative (> 30 days) valve-related adverse event rates for the model 3000TFX and the combined models 3000/3000TFX populations, respectively.

Table 7 illustrates, by valve size, hemodynamic variables reported in echocardiograms at one year performed on patients in the model 3000TFX and the combined model 3000/3000TFX studies.

Table 8 presents the change in NYHA Functional Class from baseline assessment to the 1-year visit. It should be noted that there was a 56.5% improvement in functional class at the 1-year visit for model 3000TFX. For the model 3000/3000TFX combined population, there was a 60.9% improvement in functional class at the 1-year visit.

Several published clinical studies demonstrate the long-term durability of Carpentier-Edwards PERIMOUNT pericardial aortic bioprostheses, the foundation on which the Carpentier-Edwards PERIMOUNT Magna and Magna Ease pericardial aortic bioprostheses are designed (Refs. 14, 15, 16 & 17). Additionally, published data show the PERIMOUNT Magna aortic bioprosthesis demonstrates exceptional hemodynamic performance, with a very low risk of patient-prosthesis mismatch (Refs. 18, 19, 20, 21, 22 & 23).

7. Individualization of Treatment

Bioprosthetic heart valve recipients should be maintained on anticoagulation therapy, except where contraindicated, during the initial stages after implantation as determined by the physician on an individual basis. Long-term anticoagulation and/or antiplatelet therapy should be considered for patients with risk factors for thromboembolism.

The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all the circumstances presented by that patient (Ref. 12). A bioprosthesis is recommended for AVR in patients of any age who will not take warfarin or who have major medical contraindications to warfarin therapy. Patient preference is a reasonable consideration in the selection of aortic valve operation and valve prosthesis. A mechanical prosthesis is reasonable for AVR in patients under 65 years of age who do not have a contraindication to anticoagulation. A bioprosthesis is reasonable for AVR in patients under 65 years of age who elect to receive this valve for lifestyle considerations after detailed discussions of the risks of anticoagulation versus the likelihood that a second AVR may be necessary (Ref. 12).

7.1 Specific Patient Populations

The safety and effectiveness of the Model 11000A bioprosthesis has not been established for the following specific populations because it has not been studied in these populations:

- patients who are pregnant;
- nursing mothers;
- patients with abnormal calcium metabolism (e.g., chronic renal failure, hyperparathyroidism);
- patients with aneurysmal aortic degenerative conditions (e.g., cystic medial necrosis, Marfan's syndrome);
- children, adolescents, and young adults

Caution: Based on reports in the literature on tissue valves (Refs. 6, 7, 8, 9 & 10), there appears to be an increased incidence of leaflet calcification in patients under the age of 20. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period, and excessive milk or dairy product consumption should be avoided in children. Animal research studies (Ref. 11) show that a high systemic calcium level can lead to early calcification.

8. Patient Counseling Information

Careful and continued medical follow up (at least by an annual visit to the physician) is advised so that bioprosthesis-related complications, particularly those related to material failure, can be diagnosed and properly managed. Patients with bioprostheses are at risk from bacteremia (e.g., undergoing dental procedures) and should be advised about prophylactic antibiotic therapy. Patients should be encouraged to carry their Patient Identification Card at all times and to inform their healthcare providers that they have an implant when seeking care.

9. How Supplied

9.1 Packaging

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is provided sterile and non-pyrogenic, in a double barrier tray package. The double tray package is in a foil pouch, which is in a carton.

Each bioprosthesis is contained in a carton with a temperature indicator displayed through a window on the side panel. The temperature indicator is intended to identify products that were exposed to transient temperature extremes. Upon receipt of the bioprosthesis, immediately inspect the indicator and refer to the carton label to confirm a "Use" condition. If the "Use" condition is not apparent, do not use the bioprosthesis and contact the local supplier or Edwards Lifesciences representative to make arrangements for return authorization and replacement.

Warning: Carefully inspect the bioprosthesis before implantation for evidence of extreme temperature exposure or other damage.

9.2 Storage

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, should be stored at 10 °C to 25 °C (50-77 °F), in the foil pouch and shelf carton.

10. Directions for Use

10.1 Physician Training

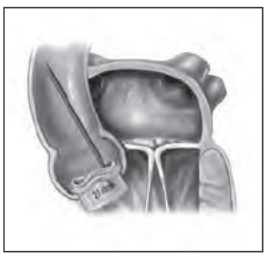
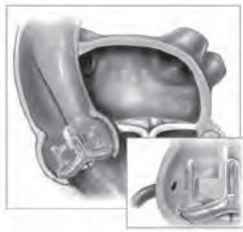
The techniques for implanting this bioprosthesis are similar to those used for supra-annular placement of any stented aortic bioprosthesis. No special training is required to implant the Edwards Pericardial Aortic Bioprosthesis, Model 11000A.

10.2 Sizing

Verify that the accessories have been sterilized according to the recommended instructions provided with the reusable accessories.

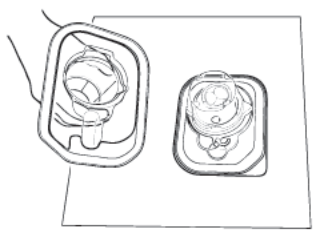
Supra-annular sizing

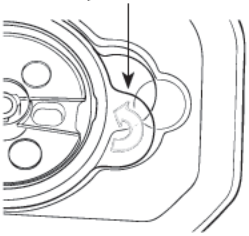
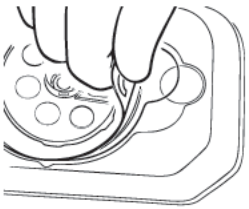
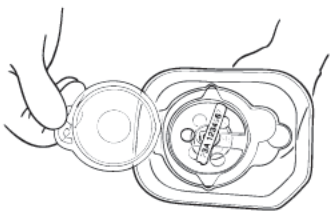
For supra-annular implantation, the sewing ring of the bioprosthesis is placed above the annulus, thereby maximizing valve orifice area. When sizing for supra-annular implantation, the sizer should be parallel with the plane of the annulus and the following sizing technique should be used:

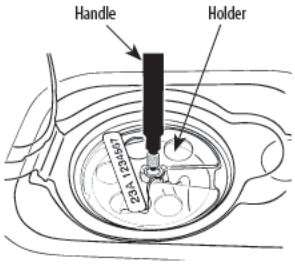
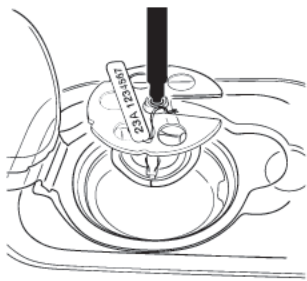
Step	Procedure
1	Using the Model 1133 sizer, select the cylindrical end of the largest diameter sizer that comfortably fits in the patient's annulus. HVT21 
2	Once the appropriate cylindrical end is verified, use the replica end of the same sizer to verify that the sewing ring will fit comfortably on top of the annulus. Ensure that the coronary ostia are not obstructed and that the stent posts of the replica end do not interfere with the aortic wall at the sinotubular junction. If satisfied with the fit of the replica end, choose this size of the bioprosthesis for implant. HVT37 

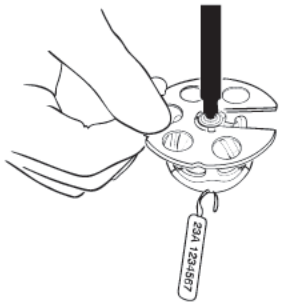
10.3 Handling and Preparation Instructions

In-service training is recommended prior to handling and preparing the Edwards Pericardial Aortic Bioprosthesis, Model 11000A.

Step	Procedure
1	**Caution: Do not open the Edwards Pericardial Aortic Bioprosthesis, Model 11000A package until implantation is certain.** **Warning: Do not open foil pouch into sterile field. Foil pouch is protective cover only. Only the innermost package tray may be introduced into the sterile field.** Once the appropriate size bioprosthesis is chosen, remove the foil pouch from the carton in the non-sterile field. Before opening, examine the package for evidence of damage and broken or missing seals.
2	Near the sterile field, hold the base of the outer tray and peel the lid from the outer tray.
3	The inner tray and contents are sterile. Transfer the inner tray to the sterile field. The contents of the inner tray must be handled using a sterile surgical technique to prevent contamination. HVT26 

Step	Procedure
4	**Caution: Do not open the inner package until implantation is certain and the surgeon is ready to place the valve.** **Caution: The bioprosthesis is not secured to the inner tray. Care should be taken while peeling the lid and opening the plastic tab.** Before opening, examine the inner tray and lid for evidence of damage, stains, and broken or missing seals. Hold the base of the inner tray and peel the lid from the inner tray.
5	To access the bioprosthesis, pull up on the plastic tab with the arrow. HVT28 Pull up on Tab with Arrow  HVT29  HVT30 

Step	Procedure
6	Attach the handle, Model 1111 or Model 1126, to the bioprosthesis holder while the bioprosthesis is still in the tray. To attach, insert the handle into the holder and turn the handle clockwise until resistance is felt. **Caution: Do not grasp the bioprosthesis with hands or surgical instruments.** **Caution: Do not push the bioprosthesis off the dip while attaching the handle to the holder.** **Caution: The handle/holder assembly is required for implantation and should not be removed until the bioprosthesis is sutured to the annulus.** **Caution: Care should be taken to avoid entangling the serial tag in the handle during attachment.** HVT31 
7	Once the handle is attached, remove the bioprosthesis and clip from the inner tray. HVT32 

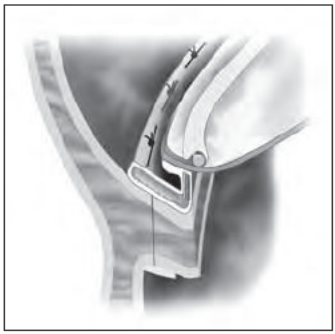
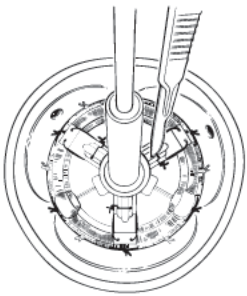
Step	Procedure
8	To remove the clip from the bioprosthesis, grasp the clip and pull away from the handle/holder assembly. HVT33  HVT34 
9	A serial number tag is attached to the sewing ring of each bioprosthesis by a suture. This serial number should be confirmed with the number on the bioprosthesis package and bioprosthesis implant data card. This tag should not be detached from the bioprosthesis until implantation is certain. **Caution: If any difference in serial number is noted, the bioprosthesis should be returned unused.** **Caution: Care should be exercised to avoid cutting or tearing the sewing ring cloth during removal of the serial number tag.** **Caution: To prevent damage to the sewing ring cloth, avoid pulling the knot of the serial tag suture through the sewing ring.**

Step	Procedure
10	The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, **DOES NOT REQUIRE RINSING** prior to implantation. **Caution: If the bioprosthesis is rinsed prior to implantation, it must then be kept hydrated with sterile physiological saline irrigation on both sides of the leaflet tissue throughout the remainder of the surgical procedure. Rinsing every one to two minutes is recommended.** **Caution: Avoid contact of the leaflet tissue with towels, linens, or other sources of particulate matter that may be transferred to the leaflet tissue.**

10.4 Device Implantation

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is designed for supra-annular implant.

Step	Procedure
1	The surgeon should be familiar with the recommendations for proper sizing and placement in the supra-annular position (See **10.2 Sizing**). Because of the complexity and variation of cardiac valve replacement surgery, the choice of surgical technique, appropriately modified in accordance with the previously described **Warnings**, is left to the discretion of the individual surgeon. In general, the following steps should be employed: 1. Surgically remove the diseased or damaged valve leaflets and all associated structures deemed necessary. 2. Surgically remove any calcium from the annulus to ensure proper seating of the sewing ring of the bioprosthesis to avoid damage to the delicate leaflet tissue. 3. Measure the annulus using only the Carpentier-Edwards aortic sizers, Model 1133 (Figures 1a-1c). **Caution: When choosing a bioprosthesis for a given patient, the size, age, and physical condition of the patient in relation to the size of the bioprosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a bioprosthesis, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient.** **Caution: Do not use other manufacturer's prosthesis sizers, or sizers for other Edwards Lifesciences bioprostheses, to size the Edwards Pericardial Aortic Bioprosthesis, Model 11000A.** **Caution: Examine sizers for signs of wear, such as dullness, cracking or crazing. Replace sizer if any deterioration is observed.** **Warning: Fragments of handles and sizers are not radio-opaque and cannot be located by means of an external imaging device.**

Step	Procedure
2	A suture technique resulting in supra-annular placement of the bioprosthesis, such as a non-everting horizontal mattress technique, should be employed. When placing sutures through the sewing ring of the Edwards Pericardial Aortic Bioprosthesis, Model 11000A, it is recommended that the sutures pass through the sewing ring as close as possible to the frame of the bioprosthesis. Once the sutures are completely tied, it is important to cut the sutures close to the knots to ensure that exposed suture tails will not come into contact with the leaflet tissue of the bioprosthesis. HVT35 
3	The integral holder and attached handle are removed as a unit at the completion of the suturing procedure. 1. Using a scalpel, cut each of the three exposed sutures that are on the top of the holder. HVT36  **Caution: Avoid cutting or damaging the stent or delicate leaflet tissue when cutting the sutures.** 2. After all three holder sutures are cut, remove the handle/holder assembly, along with the holder sutures, from the bioprosthesis as a unit. 3. Remove the handle from the holder and discard the holder.

10.5 Accessory Cleaning and Sterilization

The accessories for the Edwards Pericardial Aortic Bioprosthesis, Model 11000A, are packaged separately. The model 1126 handle is provided sterile and is intended for single use only. The model 1111 handle and model 1133 sizers are supplied nonsterile and must be sterilized before using. The handle, sizers, tray base and tray lid must be cleaned and resterilized prior to each use. Refer to the Instructions for Use supplied with the reusable accessories for cleaning and sterilization instructions.

10.6 Return of Bioprostheses

Edwards Lifesciences is interested in obtaining recovered clinical specimens of the Edwards Pericardial Aortic Bioprosthesis, Model 11000A, for analysis. Contact the local representative for return of recovered bioprostheses.

- Unopened Package with Sterile Barrier Intact: If the foil pouch or trays have not been opened, return the bioprosthesis in its original packaging.
- Package Opened but Bioprosthesis Not Implanted: If the tray is opened, the bioprosthesis is no longer sterile. If the bioprosthesis is not implanted, it should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde and returned to the company. Refrigeration is not necessary under these circumstances.
- Explanted Bioprosthesis: The explanted bioprosthesis should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde and returned to the company. Refrigeration is not necessary under these circumstances.

11. Safety in the Magnetic Resonance (MR) Environment

MR Conditional

Non-clinical testing has demonstrated that the Edwards Pericardial Aortic Bioprosthesis, Model 11000A, is MR Conditional. A patient with the model 11000A valve can be scanned safely, immediately after placement of this implant under the following conditions:

- Static magnetic field of 1.5 tesla or 3.0 tesla.
- Maximum spatial magnetic gradient field of 2670 gauss/cm.
- Maximum MR system-reported whole-body averaged specific absorption rate (SAR) of 2.0 W/kg in the normal operating mode for 15 minutes of scanning per sequence.

In non-clinical testing, the Edwards Pericardial Aortic Bioprosthesis, Model 11000A, produced an estimated maximum *in vivo* temperature rise of less than or equal to 1.8 °C at a maximum MR system reported, whole-body-averaged specific absorption rate (SAR) of 2.0 W/kg, for 15 minutes of MR scanning in a GE Signa 64 MHz (1.5 T) RF coil and a GE Signa HDx (3 T) MR system with Software Version 15\LX\MR Software release 15.0.M4.0910.a.

Image artifact was measured non-clinically in a GE Signa 3T HDx MR system according to ASTM F2119-07 using the spin echo and gradient echo sequences specified therein. The spin echo images exhibited light and dark artifacts that extended as far as 40 mm from the implant and partially to fully obscured the lumen. The gradient echo images exhibited opaque dark or light and dark triangular shaped artifacts that extended as far as 40 mm from the implant and totally obscured the lumen. Reduction in artifact may be possible with sequences designed for reduction of metal artifact.

12. Patient Information

12.1 Study Identification Card

A Study Identification Card is provided to each subject implanted with the Edwards Pericardial Aortic Bioprosthesis, Model 11000A.

12.2 Patient Information Materials

Patient information materials may be obtained from Edwards or an Edwards clinical sales specialist.

13. References

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Refer to the symbol legend at the end of this document.

Table 2. Summary of Complication Rates, Model 2700

	Isolated AVR Population			DVR Population		
Complication	**Operative % of Pts.**	**Post-Operative % Per Pt. Yr.**	**% Event-Free at Six Years (Standard Error)**	**Operative % of Pts.**	**Post-Operative % Per Pt. Yr.**	**% Event-Free at Six Years (Standard Error)**
Death	4.7	4.6	73.5 (2.0)	12.9	4.2	67.2 (6.5)
Explant	0	0.3	98.5 (1.0)	0	0.8	NA *
Valve Related Reoperation	0.7	0.1	99.8 (0.4)	0	0	NA *
All Reoperation	22.4	1.8	75.4 (1.8)	34.3	2.3	NA *
Valve Related Thromboembolism	3.1	1.5	91.4 (1.1)	1.4	5.1	NA *
All Thromboembolism	5.0	2.4	84.9 (1.6)	5.7	6.6	NA *
Endocarditis	0.6	0.8	95.8 (0.9)	1.4	1.5	NA *
Valve Dysfunction	0.1	0.7	96.0 (1.1)	0	0.4	NA *
Perivalvular Leak	0.1	0.3	98.8 (0.5)	0	1.2	NA *
Hemorrhagic Anticoagulation Complication	1.4	0.4	96.4 (1.1)	4.3	2.3	NA *
Hemolysis	0	0.2	99.1 (0.4)	0	0.4	NA *
Valve Thrombosis	0	0	100.0 (0)	0	0.4	NA *

* NA = Not Applicable

Table 3. Postoperative Echocardiography Results, Model 2700

	Valve Size						
	19 mm	**21 mm**	**23 mm**	**25 mm**	**27 mm**	**29 mm**	**Total**
Total N	12	22	15	8	3	3	63
Avg. Months Postoperative	28.6 ± 7.2	34.9 ± 8.6	36.9 ± 9.2	39.9 ± 7.6	31.4 ± 15.9	15.3 ± 12.2	34.6 ± 9.2
Velocity (M/sec)							
mean ± S.D.	2.80 ± 0.49	2.56 ± 0.46	2.36 ± 0.42	2.15 ± 0.56	2.09 ± 0.27	2.08 ± 0.1	2.46 ± 0.50
n =	12	21	15	7	3	3	61
range	1.90 - 3.60	1.90 - 3.90	1.39 - 2.86	1.00 - 2.60	1.90 - 2.40	2.05 - 2.10	1.00 - 3.90
Peak Instantaneous Gradient (mmHg)							
mean ± S.D.	32.22 ± 11.08	27.04 ± 10.49	23.00 ± 7.30	19.50 ± 8.16	17.60 ± 4.70	14.4 ± 0.58	25.67 ± 10.14
n =	12	21	15	7	3	3	61
range	14.40 - 51.80	14.40 - 60.80	7.70 - 32.70	4.00 - 27.00	14.40 - 23.00	13.95 - 15.06	4.00 - 60.80

Table 4. Effectiveness Outcomes, NYHA Functional Class, Model 2700

Preoperative NYHA Functional Class	Postoperative NYHA Functional Class					
	I	II	III	IV	Expiration	Not Available
I	18	19			9	
II	140	37			35	15
III	181	48	4	1	72	24
IV	43	16	2		53	2
Not Available	5	1			2	2

Table 5. Freedom from Complication Rates at 20 years (N = 267), Model 2700

Freedom from Complications at 20 Years	Actual	Actuarial	Linearized (%/ptyr)
Valve-Related Expirations	85.8 ± 2.5%	67.9 ± 6.6%	1.2
Thromboembolism/Thrombosis	82.4 ± 2.6%	68.2 ± 6.8%	1.7
Bleeding	94.0 ± 1.5%	91.7 ± 2.2%	0.4
Endocarditis/Sepsis	91.7 ± 1.7%	89.3 ± 2.4%	0.8
Explant due to SVD			
≥ 60	92.6 ± 2.0%	77.1 ± 7.2%	n.r.*
≥ 65	96.3 ± 1.6%	81.5 ± 9.6%	
> 70	96.0 ± 2.3%	69.9 ± 20.5%	

** Not relevant. SVD does not occur as a constant hazard function; consequently, linearized rates are not meaningful.*

Table 6. Summary of Valve-Related Adverse Events, Models 3000 and 3000TFX

	≤ 30 Days Post-Operative		> 30 Days Post-Operative	
Adverse Events	**3000TFX (N = 193) # of events (% of Pts)**	**3000/3000TFX (N = 253) # of events (% of Pts)**	**3000TFX (N = 193) # of events (% of Pts)**	**3000/3000TFX (N = 253) # of events (% of Pts)**
Valve-Related Thromboembolism	6 (3.1)	7 (2.8)	3 (2.0)	3 (1.4)
Non-Structural Valve Dysfunction (PVL)	3 (1.5)	4 (1.6)	3 (2.0)	3 (1.4)
Explant (NSVD)	2 (1.0)	2 (0.8)	0 (0.0)	0 (0.0)
Death (Cardiac Arrest, Bleeding Event, CVA)	1 (0.5)	1 (0.4)	3 (2.0)	3 (1.4)
Reoperation	1 (0.5)	1 (0.4)	1 (0.7)	1 (0.5)
Hemolysis	1 (0.5)	1 (0.4)	3 (2.0)	3 (1.4)
AC related Bleeding	0 (0.0)	0 (0.0)	2 (1.4)	2 (1.0)
Endocarditis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Structural Valve Deterioration	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Valve Thrombosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other (Tear In Aorta)	1 (0.5)	1 (0.4)	0 (0.0)	0 (0.0)

Table 7. Hemodynamic Variables at 1-Year Follow-Up Echo Assessment, Models 3000 and 3000TFX

Valve Type	Variable	19 mm Mean ± SD (N)	21 mm Mean ± SD (N)	23 mm Mean ± SD (N)	25 mm Mean ± SD (N)	27 mm Mean ± SD (N)	29 mm Mean ± SD (N)
3000TFX	Mean Systolic Gradient (mmHg)	16.7 ± 4.7 (10)	15.8 ± 4.4 (18)	11.3 ± 3.7 (45)	11.1 ± 4.1 (37)	9.4 ± 4.3 (12)	9.0 ± 0.0 (2)
	Ejection Fraction (%)	65.8 ± 10.4 (10)	62.7 ± 9.4 (19)	60.6 ± 11.3 (48)	61.4 ± 11.2 (38)	59.5 ± 10.7 (12)	55.0 ±14.1 (2)
	Aortic EOA (cm^2)	1.2 ± 0.4 (10)	1.5 ± 0.4 (18)	1.8 ± 0.6 (44)	1.8 ± 0.5 (36)	2.1 ± 0.6 (12)	2.1 ± 0.1 (2)
3000/ 3000TFX	Mean Systolic Gradient (mmHg)	16.7 ± 4.2 (16)	13.8 ± 4.8 (34)	11.7 ± 4.7 (56)	11.0 ± 3.8 (47)	9.5 ± 4.1 (14)	9.0 ± 0.0 (2)
	Ejection Fraction (%)	62.1 ± 15.1 (16)	58.6 ± 11.6 (34)	60.2 ± 11.2 (59)	60.2 ± 11.5 (47)	58.5 ± 10.5 (14)	55.0 ± 14.1 (2)
	Aortic EOA (cm^2)	1.3 ± 0.5 (16)	1.5 ± 0.4 (32)	1.8 ± 0.6 (55)	1.8 ± 0.6 (46)	2.1 ± 0.6 (14)	2.1 ± 0.1 (2)

Table 8. NYHA Functional Class: Change From Baseline To 1-Year Visit, Models 3000 and 3000TFX

		-----Baseline-----				
Valve Type	**Follow-Up NYHA Class**	**Class I**	**Class II**	**Class III**	**Class IV**	**N/A**
3000TFX N = 193	**Class I**	10	33	51	10	3
	Class II	2	8	13	2	1
	Class III	-	-	3	-	-
	Class IV	-	-	-	1	-
	Expiration	-	3	16	1	-
	Explant	-	-	3	-	-
	N/A	2	6	21	4	-
3000/ 3000TFX N = 253	**Class I**	12	40	71	11	3
	Class II	2	14	29	3	1
	Class III	-	-	3	-	-
	Class IV	-	-	1	1	-
	Expiration	-	3	19	2	-
	Explant	-	-	3	-	-
	N/A	2	7	22	4	-

NYHA Functional Class: Change From Baseline To 1-Year Visit

Valve Type	Improve N (%)	Same N (%)	Worse N (%)	N/A N (%)
3000TFX (N = 193)	109 (56.5)	22 (11.4)	2 (1.0)	60 (31.1)
3000/3000TFX (N = 253)	154 (60.9)	30 (11.9)	3 (1.2)	66 (26.1)

Français

Bioprothèse aortique péricardique d'Edwards, modèle 11000A

Mode d'emploi

AVERTISSEMENT : dispositif expérimental. Limité à une utilisation expérimentale par les lois fédérales (États-Unis).

AVERTISSEMENT : dispositif expérimental. Exclusivement à des fins de recherche clinique.

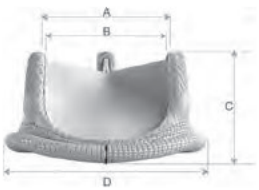
Avertissement : dispositif expérimental. Utilisation limitée à la recherche. Pour une utilisation par des (médecins) chercheurs qualifiés uniquement.

1. Description du dispositif et des accessoires

1.1 Description du dispositif

La bioprothèse aortique péricardique d'Edwards, modèle 11000A, est une bioprothèse trivalve composée d'un péricarde bovin installé sur une structure flexible. Elle est disponible en plusieurs tailles : 19, 21, 23, 25, 27 et 29 mm (tableau 1). Elle est conservée dans un emballage non aqueux et ne nécessite aucune poussée avant l'implantation.

Tableau 1 - Dimensions nominales



Taille	19 mm	21 mm	23 mm	25 mm	27 mm	29 mm
A. Diamètre de l'annulus du tissu (diamètre de l'endoprothèse, en mm)	19	21	23	25	27	29
B. Diamètre interne (D.I. de l'endoprothèse, en mm)	18	20	22	24	26	28
C. Hauteur du profil (en mm)	13	14	15	16	17	18
D. Diamètre de l'anneau de suture externe (en mm)	24	26	28	30	32	34
Surface de l'orifice (en mm^2)	235	289	354	420	499	570

Le fil métallique est fabriqué avec un alliage de chrome-cobalt et est recouvert d'un matériau tissé en polyester. Une bande laminée en alliage en chrome-cobalt/film en polyester entoure la base de la structure en fil métallique.

Un anneau de suture en silicone, qui est couvert d'un tissu poreux en polytétrafluoroéthylène (PTFE), est attaché à la structure en fil métallique. L'anneau de suture possède trois marqueurs de suture en soie noire et à distance égale aux centres de la valve pour aider à l'orientation de la bioprothèse et au placement des sutures.

Un support est attaché à la bioprothèse par suture afin de faciliter la manipulation et la suture de la bioprothèse lors de l'implantation. Le chirurgien peut facilement détacher le support (voir la section **10.4 Implantation du dispositif**).

1.2 Description des accessoires

Calibreurs et plateau

L'utilisation d'un instrument de mesure permet de sélectionner facilement la bioprothèse de taille appropriée pour l'implantation. Les calibreurs translucides, modèle 1133, permettent une observation directe du placement dans l'annulus. Chaque calibreur comprend une poignée dotée d'une configuration de mesure différente à chaque extrémité (figure 1a). Sur l'une des extrémités de la poignée se trouve un embout cylindrique doté d'une lèvre reprenant la forme géométrique de l'anneau de suture de la bioprothèse (figure 1b). Sur l'autre extrémité se trouve un embout de réplique de la bioprothèse qui reprend la forme de l'anneau de suture de la bioprothèse ainsi que la hauteur et l'emplacement des montants de l'endoprothèse (figure 1c). Un calibreur est disponible pour chaque taille de la bioprothèse de modèle 11000A (19, 21, 23, 25, 27 et 29 mm). La trousse complète de calibreurs se trouve dans un plateau, modèle TRAY1133, qui peut être réutilisé et restérilisé.

Figure 1a. Calibreur aortique

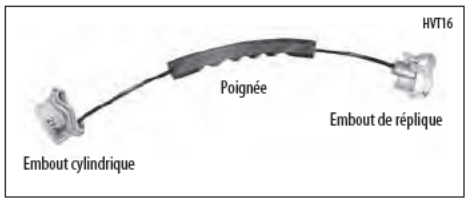


Figure 1b. Embout cylindrique

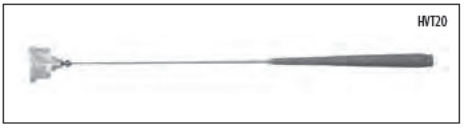
Figure 1c. Embout de réplique

Poignée et support de la bioprothèse

L'assemblage poignée/support est constitué de deux composants : une partie jetable intégrable qui est installée sur la bioprothèse par le fabricant et une poignée malléable (modèle 1111 réutilisable ou modèle 1126 jetable pour utilisation unique) qui est attachée au suppor au moment de la chirurgie (figures 2a et 2b).

Figure 2a. Poignée du modèle 1111

Figure 2b. Poignée du modèle 1126



2. Mode d'emploi

La bioprothèse aortique péricardique d'Edwards, modèle 11000A, est destinée aux patients nécessitant le remplacement de leur valve aortique d'origine ou prothétique.

3. Contre-indications

Ne pas utiliser la bioprothèse si le chirurgien estime que son utilisation est contraire à l'intérêt du patient. La décision concernant cette bioprothèse relève du chirurgien qui doit évaluer tous les risques impliqués, y compris l'anatomie et la pathologie observées au moment de l'opération chirurgicale.

4. Mises en garde

POUR UTILISATION UNIQUE SEULEMENT. Ce dispositif est conçu, destiné et distribué pour une utilisation unique seulement. Ne pas restériliser ou réutiliser ce dispositif. Aucune donnée n'existe pour corroborer le caractère stérile, la non-pyrogénicité et la fonctionnalité du dispositif après le processus de restérilisation.

NE PAS CONGELER NI EXPOSER LA BIOPROTHÈSE À UNE CHALEUR EXTRÊME. L'exposition de la bioprothèse à des températures extrêmes rendra le dispositif inutilisable.

NE PAS UTILISER la bioprothèse :

- **si le sachet métallisé, les plateaux scellés ou les lèvres sont ouverts, endommagés ou tachés ;**
- **si la date d'expiration est passée ;**
- **si elle est tombée, endommagée ou mal manipulée de quelque façon que ce soit. Si une bioprothèse est endommagée lors de l'insertion, ne pas tenter de la réparer.**

NE PAS EXPOSER la bioprothèse à des solutions, des produits chimiques, des antibiotiques, etc., à l'exception de solutions salines physiologiques. Des dommages irréparables, qui ne semblent peut-être pas apparents lors d'une inspection visuelle, peuvent avoir lieu sur le tissu de la valve.

NE PAS SAISIR le tissu de la valve de la bioprothèse avec des instruments ni endommager la bioprothèse. Même la plus petite perforation du tissu de la valve peut s'agrandir à terme et compromettre gravement le fonctionnement de la bioprothèse.

NE PAS CHOISIR UNE TAILLE SUPÉRIEURE. Le choix d'une taille supérieure peut entraîner des dommages à la bioprothèse ou un stress mécanique localisé, susceptible de blesser le cœur ou de causer une panne du tissu de la valve, une distorsion de l'endoprothèse ou une régurgitation du tissu de la valve.

Comme pour tout dispositif médical implanté, il existe un risque de réponse d'immunisation de la part du patient. Certains composants du modèle 11000A sont en alliage contenant du cobalt, du chrome, du nickel, du molybdène, du manganèse, du carbone, du béryllium et du fer. Il faut prendre des précautions avec les patients souffrant d'hypersensibilité à ces matières. Ce dispositif ne contient pas de latex mais peut avoir été fabriqué dans un environnement qui en contient.

5. Événements indésirables

5.1 Événements indésirables observés

Comme pour toutes les valvules cardiaques prothétiques, des événements indésirables graves pouvant parfois aller jusqu'au décès peuvent être associés à l'utilisation de valvules tissulaires. En outre, des événements indésirables découlant de la réaction du patient au dispositif implanté ou encore d'une modification physique ou chimique de ses composants, plus particulièrement de ceux dont l'origine est biologique, peuvent survenir à des intervalles variables (allant de plusieurs heures à plusieurs jours) et nécessitent une nouvelle opération pour remplacer la prothèse.

La conception de la bioprothèse aortique péricardique d'Edwards, modèle 11000A, est similaire à celle des bioprothèses péricardiques PERIMOUNT Magna Ease du modèle 3300TFX de Carpentier-Edwards.

Les événements indésirables associés à l'utilisation de bioprothèses péricardiques PERIMOUNT de Carpentier-Edwards et compilés à partir de documentation et de rapports provenant du système de surveillance du produit, conformément aux dispositions réglementaires américaines (fédérales) régissant les bonnes pratiques de fabrication (Good Manufacturing Practices, section 820.198), incluent la sténose, la régurgitation par une valve insuffisante, la fuite périvalvulaire, l'endocardite, l'hémolyse, la thrombo-embolie, l'obstruction thrombotique, la diathèse hémorragique associée à l'utilisation d'une anticoagulothérapie et la dysfonction de la valvule découlant d'une déformation de l'implant, d'une rupture du fil métallique ou d'une détérioration physique ou chimique des éléments de la valvule. Les types de détérioration des tissus pouvant survenir sont l'infection, la calcification, l'amincissement, la perforation, la dégénérescence, l'abrasion de la suture, le trauma causé par un instrument et le détachement de la valve des montants de l'endoprothèse. Ces complications peuvent se manifester de façon clinique, sous forme, par exemple, de souffle cardiaque anormal, d'essoufflement, d'intolérance à l'exercice, de dyspnée, d'orthopnée, d'anémie, de fièvre, d'arythmie, d'hémorragie, d'accident ischémique transitoire, d'accident vasculaire cérébral, de paralysie, de débit cardiaque faible, d'œdème pulmonaire, d'insuffisance cardiaque congestive, d'insuffisance cardiaque et d'infarctus du myocarde.

Remarque : selon des rapports issus de documentation sur des valvules tissulaires (réfs. 6, 7, 8, 9 et 10), la fréquence des calcifications de la valve serait supérieure chez les patients de moins de 20 ans. À cet égard, les recherches effectuées sur les animaux (réf. 11) démontrent qu'un niveau élevé de calcium dans le système peut entraîner une calcification précoce. En outre, au moins un rapport publié décrit la relation possible entre la consommation quotidienne de compléments de calcium et la calcification précoce de la valve chez l'adulte (réf. 13). Lorsque cela est possible, il faut éviter les injections intraveineuses répétées contenant du calcium pendant la période postopératoire. Parallèlement, la consommation excessive de lait ou de produits laitiers doit être évitée chez l'enfant. Il n'existe aucune donnée clinique démontrant la résistance accrue de la bioprothèse aortique péricardique d'Edwards, modèle 11000A, à la calcification, par rapport aux autres bioprothèses du marché.

5.2 Événements indésirables potentiels

Les événements indésirables potentiels associés à l'utilisation de biovalvules cardiaques prothétiques sont les suivants :

- Angine de poitrine
- Diathèse hémorragique (coagulopathie) en lien avec l'anticoagulothérapie
- Arythmie cardiaque
- Blocage de la valvule ostiale coronaire
- Endocardite
- Insuffisance cardiaque
- Hémolyse
- Anémie hémolytique
- Hémorragie
- Infection locale et systémique
- Infarctus du myocarde
- Inadaptation de la prothèse au patient
- Enclavement de la valve prothétique (coincement)
- Dysfonction non structurelle de la prothèse
- Pannus de la prothèse
- Fuite périvalvulaire de la prothèse
- Régurgitation de la prothèse
- Détérioration de la structure de la prothèse
- Thrombose prothétique
- Accident vasculaire cérébral
- Thrombo-embolie
- Insuffisance cardiaque congestive

Ces complications peuvent avoir les conséquences suivantes :

- Nouvelle opération chirurgicale
- Explantation
- Handicap permanent
- Décès

6. Études cliniques

Cohorte de patients avec approbation préalable

Des données cliniques sur 719 patients ayant besoin isolément d'un remplacement de la valvule aortique (RVA) par la bioprothèse péricardique PERIMOUNT de Carpentier-Edwards, modèle 2700, avec suivi moyen de 3,9 années, indiquent un taux de survie global (calcul actuariel) de 73,7 % ± 2 % à la 6e année. Les données cliniques provenant de 70 patients ayant besoin d'un remplacement double de la valvule (RDV) avec suivi moyen de 3,7 années, indiquent un taux de survie global (calcul actuariel) de 67,2 % ± 6,5 % à la 6e année. Ces données sur une cohorte de patients avec approbation préalable ont été recueillies dans la période allant d'août 1981 à janvier 1989.

La population ayant subi isolément un RVA comprenait un total de 455 hommes (63,3 %) et de 264 femmes (36,7 %). Leur âge moyen (± l'écart-type) au moment de l'implantation était de 64 ans (± 12,4), et ils étaient âgés de 18 à 90 ans. Les indications pour le remplacement de la valvule étaient la sténose (63,4 %), la régurgitation (16,3 %), des maladies mixes (15,3 %) et une dysfonction de la valvule aortique prothétique (5 %).

La population ayant subi un RDV comprenait un total de 24 hommes (34,3 %) et de 46 femmes (65,7 %). L'âge moyen (± l'écart-type) était de 62,9 ans (± 12,7), et ils étaient âgés de 31 à 94 ans. Les indications pour le remplacement de la valvule étaient la sténose (45,7 %), la régurgitation (25,7 %), des maladies mixes (21,4 %) et une dysfonction de la valvule aortique prothétique (7,4 %).

Les méthodes de suivi incluaient des visites à l'hôpital, des visites au cabinet et des communications par téléphone ou par lettre avec le patient, sa famille ou le médecin.

Le tableau 2 récapitule les taux de complications opératoires et postopératoires pour la population avec RVA isolé et pour la population ayant subi un RDV. Les taux de complications opératoires proviennent de 719 patients de la population ayant subi un RVA isolé et de 70 patients de la population ayant subi un RDV. Les taux de complications postopératoires se basent sur un suivi de 2767,9 et 255,8 années ayant eu lieu plus de 30 jours après les implantations chez la population ayant subi un RVA isolé et chez la population ayant subi un RDV, respectivement.

Le tableau 3 présente les résultats de l'échocardiographie postopératoire des patients de la population de cette étude, par taille de valvule.

Les données sur la classification fonctionnelle préopératoire et postopératoire de la NYHA ont été recueillies pour la population ayant subi isolément un RVA. La classification fonctionnelle de la NYHA n'a pas été mentionnée pour 220 patients (171 patients décédés et 49 patients non disponibles). En ce qui concerne les 499 patients pour lesquels la classification fonctionnelle préopératoire et postopératoire de la NYHA a été mentionnée lors du dernier suivi disponible, la situation s'était empirée pour 10 d'entre eux (2 %), était inchangée pour 59 d'entre eux (11,8 %) et s'était améliorée pour 430 d'entre eux (86,2 %).

Le tableau 4 présente une comparaison des données de la classification fonctionnelle préopératoire de la NYHA avec celles de la classification postopératoire lors du dernier suivi.

Cohorte de patients avec approbation postérieure

Depuis novembre 1981, Edwards a suivi une cohorte approuvée postérieurement de 267 patients ayant subi un remplacement de la valvule (RVA) (modèle 2700), provenant de quatre centres de l'étude clinique d'origine de la bioprothèse péricardique PERIMOUNT de Carpentier-Edwards. Cette population était constituée de 171 hommes (64 %) et de 96 femmes (36 %). Leur âge moyen (± écart-type) au moment de l'implantation était de 64,9 ans ± 11,8 ans, et ils étaient âgés de 21 à 86 ans. En tout, 2407 années-patient de données étaient disponibles pour l'analyse (2386 d'années-patient tardives). Le suivi moyen était de 9 ± 5,5 ans, avec un maximum de 20,3 ans. En tout, on compte 189 décès entre 1981 et 1994, dont 48 (25,3 %) en lien établi avec la valvule. Les méthodes de suivi utilisées par chaque clinique incluaient des visites à l'hôpital, des visites au cabinet et des communications par téléphone ou par lettre avec le patient, sa famille ou le médecin.

Le tableau 5 résume la latitude découlant des taux de complications après 20 ans. La situation des patients à partir du dernier intervalle de suivi incluait 189 décédés (70,8 %), 10 vivants (3,8 %), 46 ayant subi une explantation (17,2 %) et 22 ayant quitté le suivi (8,2 %).

Cette population comptait 48 décès en lien avec la valvule. Un décès en lien avec la valvule est survenu au cours de la période de l'opération, par saignement. Sur les 28 décès postopératoires en lien avec la valvule, 5 découlaient de thrombo-embolie, 4 d'endocardite/sepsie, 3 de détérioration de la structure de la valvule et 1 de saignement. Quinze autres décès ont été associés à la valvule à cause du manque d'information, ou parce qu'ils ont été classés ainsi par le chercheur. Le calcul actuariel de la latitude des décès liés à la valvule donne 67,9 ± 6,6 % après 20 ans. Enfin, 19 autres décès sont reliés à une cause inconnue ou à une

mort subite, et pourraient avoir un lien avec la valvule. Par prudence, ces décès sont associés à la valvule. Par conséquent, la latitude actuarielle qui en découle pour les décès en lien avec la valvule sont de 55,4 ± 6,4 % après 20 ans.

Une amélioration dans la classification fonctionnelle de la NYHA a également été démontrée dans la période postopératoire. Jusqu'à l'évaluation du dernier suivi, 108 patients (44,8 %) faisaient partie de la classe fonctionnelle I de la NYHA.

Ces données sont été compilées à partir d'un essai clinique multicentre effectué par Edwards Lifesciences. Pour en savoir plus sur cet essai, communiquez avec Edwards Lifesciences S.A.R.L., Heart Valve Therapy Marketing Department, One Edwards Way, Irvine, CA 92614-5686.

Étude de confirmation

Entre les mois d'août 2003 et janvier 2004, 60 patients ayant besoin d'un remplacement de la valvule aortique (RVA) se sont vus implanter la bioprothèse aortique Magna PERIMOUNT de Carpentier-Edwards (modèle 3000) dans cinq établissements (deux en Europe et trois au Canada). Peu de temps après, le protocole a été modifié en vue d'autoriser l'implantation de la bioprothèse aortique Magna PERIMOUNT de Carpentier-Edwards (modèle 3000TFX), et d'ajouter trois établissements américains. Par la suite, 193 autres patients se sont vus implanter le modèle 3000TFX entre décembre 2004 et décembre 2006. À la différence du modèle 3000, le modèle 3000TFX est traité par le biais du processus ThermaFix.

La population ayant reçu le modèle 3000TFX comprenait un total de 116 hommes (60,1 %) et de 77 femmes (39,9 %). L'âge moyen au moment de l'implantation était de 72 ans (écart-type de ± 8,59) et ils étaient âgés de 26 à 89 ans. La principale indication pour le remplacement de la valvule était la sténose (78,2 %), suivie des maladies mixtes (14,5 %) et de la régurgitation (7,3 %).

La population ayant reçu les modèles 3000 et 3000TFX comprenait un total de 150 hommes (59,3 %) et de 103 femmes (40,7 %). L'âge moyen au moment de l'implantation était de 72,2 ans (écart-type de ± 8,31) et ils étaient âgés de 26 à 89 ans. Ici encore, la principale indication pour le remplacement de la valvule était la sténose (77,5 %), suivie des maladies mixtes (15,4 %) et de la régurgitation (7,1 %).

Les patients étaient évalués avant l'opération, pendant l'opération, lors de la sortie, entre 3 et 6 mois, après un an, et chaque année par la suite. Le suivi cumulatif pour le modèle 3000TFX était de 167 années-patient, pour un suivi moyen de 0,9 année (écart-type = 0,42, plage = 0 à 2,1 années). Le suivi cumulatif pour les modèles 3000 et 3000TFX combinés était de 232 années-patient, avec un suivi moyen de 0,9 année (écart-type = 0,42, plage = 0 à 2,1 années).

Le tableau 6 récapitule les taux d'événements indésirables en lien avec la valvule et survenus au début (≤ 30 jours) et à la fin (> 30 jours) de la période postopératoire dans les populations ayant reçu le modèle 3000TFX et les modèles 3000 et 3000TFX combinés, respectivement.

Le tableau 7 illustre, par taille de valvule, les variables hémodynamiques signalées dans les échocardiogrammes effectués après un an chez les patients des études sur le modèle 3000TFX et sur les modèles 3000 et 3000TFX combinés.

Le tableau 8 présente le changement de classe fonctionnelle de la NYHA par rapport à l'évaluation de base de la visite après un an. Il convient de remarquer qu'une amélioration de 56,5 % a été signalée lors de la visite de un an dans la classification fonctionnelle de la population portant le modèle 3000TFX. En ce qui concerne les modèles 3000 et 3000TFX combinés, on constate une amélioration de 60,9 % dans la classification fonctionnelle au bout d'un an.

Plusieurs études cliniques ayant été publiées démontrent la durabilité à long terme des bioprothèses aortiques péricardiques PERIMOUNT de Carpentier-Edwards, qui constituent la base sur laquelle les bioprothèses aortiques péricardiques Magna et Magna Ease PERIMOUNT de Carpentier-Edwards sont conçues (réfs. 14, 15, 16 & 17). De plus, des données publiées prouvent que la bioprothèse aortique Magna PERIMOUNT a un rendement hémodynamique exceptionnel et ne présente qu'un risque très réduit d'inadaptation de la prothèse au patient (réfs. 18, 19, 20, 21, 22 & 23).

7. Individualisation du traitement

Sauf indication contraire, les destinataires de la valvule bioprothétique doivent suivre une anticoagulothérapie pendant les premiers stades suivant l'implantation, selon les consignes données à chacun par le médecin. Une anticoagulothérapie ou un traitement antiplaquettaire doit être envisagé pour les patients montrant des facteurs de risque de thrombo-embolie.

Le jugement final concernant les soins pour un patient donné doit être pris par le fournisseur de santé et le patient à la lumière de l'ensemble de la situation que présente ce dernier (réf. 12). Il est recommandé de poser une bioprothèse en cas de RVA sur des patients de tous âges qui ne prennent pas de warfarine ou pour lesquels il existe une contre-indication importante à la thérapie à base de warfarine. Les préférences du patient sont également à prendre en compte dans une mesure raisonnable lors du choix de l'opération de la valvule aortique et de la valve prothétique. Il est raisonnable d'envisager l'implantation d'une prothèse mécanique pour un RVA de patients de moins de 65 ans pour lesquels l'anticoagulation n'est pas contre-indiquée. Il est également raisonnable d'envisager l'implantation d'une bioprothèse pour un RVA de patients de moins de 65 ans qui ont fait ce choix pour des raisons de mode de vie après avoir été informés dans les détails des risques de l'anticoagulation par rapport à l'éventuelle nécessité d'un deuxième RVA (réf. 12).

7.1 Populations de patients spécifiques

L'innocuité et l'efficacité de la bioprothèse 11000A n'ont pas été établies pour les populations suivantes, sur lesquelles elles n'ont pas été étudiées :

- patientes enceintes ;
- mères qui allaitent ;
- patients métabolisant le calcium de manière anormale (p. ex., insuffisance rénale, hyperparathyroïdisme) ;
- patients présentant une insuffisance dégénérative anévrismale de l'aorte (p. ex., nécrose médiale kystique, syndrome de Marfan) ;
- enfants, adolescents et jeunes adultes.

Avertissement : selon des rapports issus de documentation sur des valvules tissulaires (réfs. 6, 7, 8, 9 et 10), la fréquence des calcifications de la valve serait supérieure chez les patients de moins de 20 ans. Lorsque cela est possible, il faut éviter les injections intraveineuses répétées contenant du calcium pendant la période postopératoire. Parallèlement, la consommation excessive de lait ou de produits laitiers doit être évitée chez l'enfant. À cet égard, les recherches effectuées sur les animaux (réf. 11) démontrent qu'un niveau élevé de calcium dans le système peut entraîner une calcification précoce.

8. Informations et conseils au patient

Il est conseillé de procéder à un suivi sérieux et continu (au moins par une visite annuelle chez le médecin) afin que les complications liées à la bioprothèse, et plus particulièrement aux problèmes de matériau, puissent faire l'objet d'un diagnostic et d'un traitement adaptés. Les patients porteurs de bioprothèses sont vulnérables à la bactériémie (p. ex., lors de procédures dentaires) et doivent recevoir des conseils concernant l'antibioprophylaxie. Enfin, il faut encourager les patients à porter en permanence leur carte d'identification et d'informer les fournisseurs dont ils sollicitent des soins qu'ils possèdent un implant.

9. Présentation

9.1 Conditionnement

La bioprothèse aortique péricardique d'Edwards, modèle 11000A, est fournie stérile et non pyrogène. Elle est livrée dans un emballage de plateau à double barrière placé dans un sachet métallisé, se trouvant lui-même dans un carton.

Chaque bioprothèse se trouve dans un carton avec un indicateur de température visible à travers une fenêtre sur le panneau latéral. Cet indicateur vise à repérer les produits exposés à des températures extrêmes transitoires. À la réception de la bioprothèse, inspecter immédiatement l'indicateur et consulter l'étiquette du carton pour confirmer l'état « Utiliser ». Si l'état « Utiliser » n'est pas apparent, ne pas se servir de la bioprothèse et contacter le fournisseur local ou le représentant d'Edwards Lifesciences pour prendre des arrangements en vue d'une autorisation de retour et d'un remplacement.

Mise en garde : inspecter soigneusement la bioprothèse avant l'implantation pour trouver des traces d'exposition à des températures extrêmes ou d'autres dégâts.

9.2 Stockage

La bioprothèse aortique péricardique d'Edwards, modèle 11000A, doit être entreposée à une température comprise entre 10 °C et 25 °C (50 °F et 77 °F), dans son sachet métallisé et son carton de rangement.

10. Directives d'utilisation

10.1 Formation du médecin

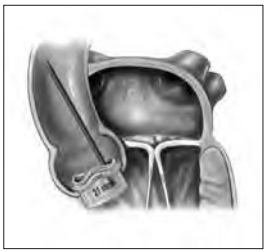
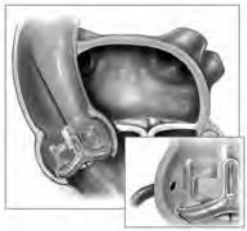
Les techniques d'implantation de cette bioprothèse sont semblables à celles du placement supra-annulaire de n'importe quelle bioprothèse aortique avec endoprothèse. Aucune formation particulière n'est nécessaire pour implanter la bioprothèse aortique péricardique d'Edwards, modèle 11000A.

10.2 Choix de la taille

Vérifier que les accessoires ont été stérilisés conformément aux recommandations fournies avec les articles réutilisables.

Mesure supra-annulaire

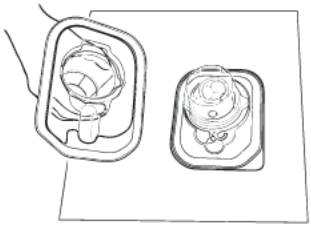
Pour l'implantation supra-annulaire, l'anneau de suture de la bioprothèse est placé au-dessus de l'annulus, maximisant ainsi la zone de l'orifice de la valve. Lors de la mesure pour une implantation supra-annulaire, le calibreur doit être placé parallèlement au plan de l'annulus et il faut utiliser la technique de mesure suivante :

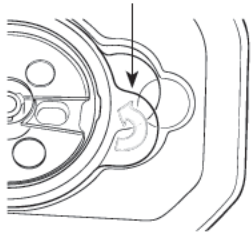
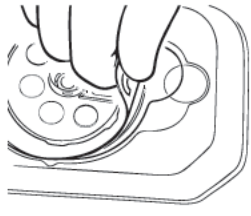
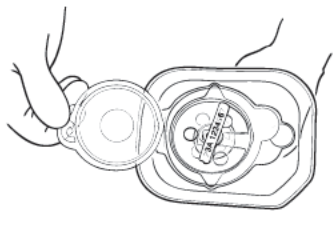
Étape	Procédure
1	À l'aide du calibreur de modèle 1133, sélectionner l'embout cylindrique du calibreur ayant le diamètre le plus large qui s'adapte confortablement dans l'annulus du patient. HVT21 
2	Une fois que l'embout cylindrique approprié a été vérifié, utiliser l'embout de réplique du même calibreur afin de vérifier que l'anneau de suture s'adapte bien sur le dessus de l'annulus. S'assurer que l'ostium coronaire n'est pas bloqué et que les montants de l'endoprothèse du bout de réplique n'interfèrent pas avec la paroi aortique à la jonction sinotubulaire. Si l'embout de réplique convient, choisir cette taille de bioprothèse pour l'implantation. HVT37 

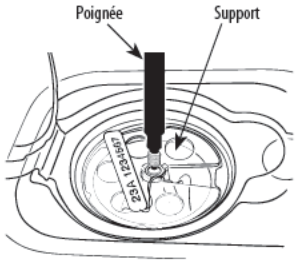
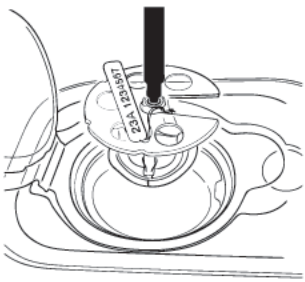
10.3 Instructions de manipulation et de préparation

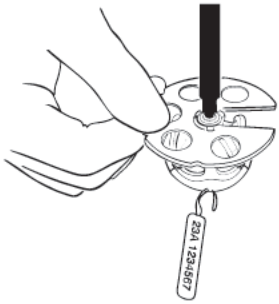
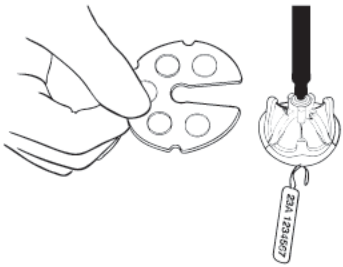
Il est conseillé de suivre une formation sur le tas avant de manipuler et de préparer la bioprothèse aortique péricardique d'Edwards, modèle 11000A.

Étape	Procédure
1	**Avertissement : ne pas ouvrir pas l'emballage du modèle 11000A de la bioprothèse aortique péricardique d'Edwards avant d'avoir l'assurance que l'implantation aura lieu.** **Mise en garde : Ne pas ouvrir le sachet métallisé dans une zone stérile. Ce sachet ne sert qu'à protéger la bioprothèse. Seul l'emballage le plus à l'intérieur peut pénétrer dans la zone stérile.** Une fois que la bonne taille de bioprothèse a été choisie, retirer le sachet métallisé du carton dans la zone non stérile. Avant d'ouvrir, examiner l'emballage pour vérifier s'il y a des dommages et des scellés cassés ou manquants.
2	Près de la zone stérile, tenir la base du plateau extérieur et retirer son couvercle.

Étape	Procédure
3	Le plateau intérieur et son contenu sont stériles. Transférer le plateau interne sur la zone stérile. Le contenu du plateau intérieur doit être manipulé en utilisant une technique chirurgicale stérile afin d'empêcher la contamination. HVT26 
4	**Avertissement : ne pas ouvrir pas l'emballage intérieur avant d'avoir l'assurance que l'implantation aura lieu et que le chirurgien est prêt à mettre la valvule en place.** **Avertissement : la bioprothèse n'est pas fixée sur le plateau intérieur. Il faut faire attention en ouvrant le couvercle et en tirant sur la languette en plastique.** Avant d'ouvrir, examiner le plateau intérieur et le couvercle pour vérifier s'il y a des dommages, des tâches et des scellés cassés ou manquants. Tenir la base du plateau intérieur et retirer son couvercle.

Étape	Procédure
5	Pour accéder à la bioprothèse, tirer sur la languette en plastique avec la flèche. HVT28  HVT29  HVT30 

Étape	Procédure
6	Fixer la poignée (modèle 1111 ou 1126) au support de la bioprothèse alors que cette dernière se trouve toujours dans le plateau. Pour la fixer, insérer la poignée sur le support et la tourner vers la droite jusqu'à sentir une résistance. **Avertissement : ne pas saisir la bioprothèse avec les mains ou des instruments chirurgicaux.** **Avertissement : ne pas retirer la bioprothèse du dip lorsque la poignée est fixée au support.** **Avertissement : l'assemblage poignée/support est nécessaire à l'implantation et ne doit pas être retiré jusqu'à ce que la bioprothèse soit suturée sur l'annulus.** **Avertissement : il faut éviter d'enchevêtrer l'étiquette avec le numéro de série dans la poignée lors de la fixation.** HVT31 
7	Une fois la poignée fixée, retirer la bioprothèse et le clip du plateau intérieur. HVT32 

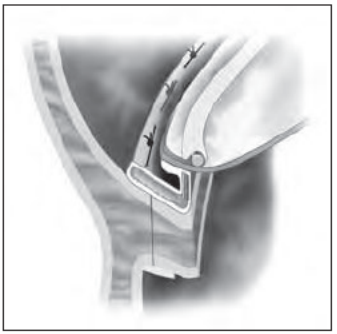
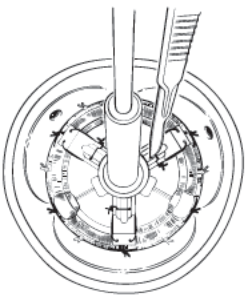
Étape	Procédure
8	Pour retirer le clip de la bioprothèse, saisir le clip et le retirer de l'assemblage poignée/support. HVT33  HVT34 
9	Une étiquette avec le numéro de série est fixée à l'anneau de suture de chaque bioprothèse par une suture. Ce numéro de série doit être comparé avec le numéro se trouvant sur l'emballage de la bioprothèse et sur la carte de données d'implantation de la bioprothèse. L'étiquette ne doit pas être détachée de la bioprothèse jusqu'à ce que l'implantation soit sûre. **Avertissement : si les numéros de série sont différents, la bioprothèse doit être renvoyée sans avoir été utilisée.** **Avertissement : il faut faire attention en coupant ou déchirant le tissu de l'anneau de suture lorsque l'étiquette du numéro de série est retirée.** **Avertissement : pour éviter d'endommager le tissu de l'anneau de suture, ne pas tirer sur la suture à travers l'anneau.**

Étape	Procédure
10	**IL EST INUTILE DE RINCER** la bioprothèse aortique péricardique d'Edwards, modèle 11000A, avant l'implantation. **Avertissement : si la bioprothèse est rincée avant l'implantation, elle doit être ensuite conservée hydratée à l'aide d'une irrigation saline physiologique stérile sur les deux côtés du tissu de la valve pendant toute la durée de la procédure chirurgicale. Il est recommandé de la rincer toutes les une à deux minutes.** **Avertissement : éviter que le tissu de la valve entre en contact avec des serviettes, des linges ou d'autres sources de particules susceptibles de s'y transférer.**

10.4 Implantation du dispositif

La bioprothèse aortique péricardique d'Edwards, modèle 11000A, est conçue pour une implantation supra-annulaire.

Étape	Procédure
1	Le chirurgien doit être familier avec les recommandations concernant la mesure et le positionnement supra-annulaire (voir la section **10.2 Choix de la taille.**) À cause de la complexité et de la variété du remplacement chirurgical de la valve cardiaque, le choix de la technique chirurgicale, correctement modifiée selon les **mises en garde** décrites précédemment, est à la discrétion du chirurgien individuel. En général, les étapes suivantes doivent être suivies : 1. Retirer par chirurgie les valves malades ou endommagées ainsi que toutes les structures associées au besoin. 2. Retirer par chirurgie le calcium de l'annulus afin d'assurer un bon positionnement de l'anneau de suture de la bioprothèse pour éviter d'endommager le tissu délicat de la valve. 3. Mesurer l'annulus à l'aide des calibreurs aortiques Carpentier-Edwards de modèle 1133 (figures 1a-1c). **Avertissement : lors d'un choix d'une bioprothèse, il faut prendre en compte la taille, l'âge et l'état physique par rapport à la taille de la bioprothèse, afin de minimiser le risque d'hémodynamique sous-optimale. Toutefois, le choix final revient au médecin individuellement après l'évaluation des risques et des avantages pour le patient.** **Avertissement : ne pas utiliser les calibreurs de prothèse d'autres fabricants ou des calibreurs de toute autre bioprothèse Edwards Lifesciences pour mesurer la bioprothèse aortique péricardique d'Edwards, modèle 11000A.** **Avertissement : vérifier si les calibreurs contiennent des traces d'eau, telles que des ternissures, des fissurations ou des craquelures. Remplacer le calibreur si des détériorations sont observées.** **Mise en garde : les fragments des poignées et des calibreurs ne sont pas radio-opaques et ne peuvent pas être trouvés par un imageur externe.**

Étape	Procédure
2	Il faut utiliser une technique de suture pour l'emplacement de l'annulus supérieur de la bioprothèse, telle que la technique du matelas horizontal à point simple interrompu. En cas de suture dans l'anneau de suture de la bioprothèse aortique péricardique d'Edwards, modèle 11000A, il est recommandé que les sutures passent dans l'anneau de suture aussi près que possible de la structure de la bioprothèse. Une fois que les sutures sont entièrement nouées, il est important de couper les sutures près des nœuds pour s'assurer que les fils de suture exposés n'entrent pas en contact avec le tissu de la valve de la bioprothèse. HVT35 
3	Le support intégral et la poignée attachée sont retirés comme une unité à la fin de la procédure de suture. 1. À l'aide d'un scalpel, couper chacune des trois sutures exposées qui se trouvent sur le dessus du support. HVT36  **Avertissement : éviter de couper ou d'endommager l'endoprothèse ou le tissu délicat de la valve lorsque les sutures sont coupées.** 2. Après avoir coupé les trois sutures du support, retirer ensemble l'assemblage poignée/support, ainsi que les sutures du support, de la bioprothèse. 3. Retirer la poignée du support et jeter ce dernier.

10.5 Nettoyage et stérilisation des accessoires

Les accessoires de la bioprothèse aortique péricardique d'Edwards, modèle 11000A, sont emballés à part. La poignée du modèle 1126 est stérile et est destinée à un usage unique. La poignée du modèle 1111 et les calibreurs du modèle 1133 ne sont pas stériles et doivent être stérilisés avant l'utilisation. Les poignées, les calibreurs, la base et le couvercle du plateau doivent être nettoyés et restérilisés avant chaque utilisation. Consulter le mode d'emploi fourni avec les accessoires réutilisables pour connaitre les consignes de nettoyage et de stérilisation.

10.6 Retour de la bioprothèse

Edwards Lifesciences est intéressé à obtenir des échantillons cliniques recouverts de la bioprothèse aortique péricardique d'Edwards, modèle 11000A, à des fins d'analyse. Pour retourner des bioprothèses recouvertes, contacter votre représentant.

- Emballage non ouvert avec la barrière stérile intacte : si le sachet métallisé ou les plateaux n'ont pas été ouverts, retourner la bioprothèse dans son emballage d'origine.
- Emballage ouvert, mais avec la bioprothèse non implantée : si le plateau est ouvert, la bioprothèse n'est plus stérile. Si la bioprothèse n'est pas implantée, elle doit être placée dans un fixateur histologique adapté comme di formaldéhyde à 10 % ou du glutaraldéhyde à 2 %, puis retournée à l'entreprise. La réfrigération n'est pas nécessaire dans ces circonstances.
- Bioprothèse explantée : la bioprothèse explantée doit être placée dans un fixateur histologique adapté comme di formaldéhyde à 10 % ou du glutaraldéhyde à 2 %, puis retournée à l'entreprise. La réfrigération n'est pas nécessaire dans ces circonstances.

11. Sécurité dans l'environnement de résonance magnétique (RM)

Condition RM

Des tests non cliniques ont montré que la bioprothèse aortique péricardique d'Edwards, modèle 11000A, est conforme à la condition RM. Un patient la possédant peut subir un balayage sans danger immédiatement après l'implantation, dans les conditions suivantes :

- Champ magnétique statique de 1,5 ou 3 tesla.
- Gradient de champ magnétique spatial maximum de 2670 gauss/cm.
- Taux d'absorption spécifique moyen signalé par le système RM pour tout le corps de 2 W/kg en mode de fonctionnement normal pour un balayage de 15 par séquence.

En essai non clinique, la bioprothèse aortique péricardique d'Edwards, modèle 11000A, a produit une élévation maximale estimée de température *in vivo* inférieure ou égale à 1,8 °C à un taux d'absorption spécifique moyen signalé par le système RM pour tout le corps de 2 W/kg en mode de fonctionnement normal pour un balayage de 15 par séquence, dans un circuit RF Signa de GE de 64 MHz (1,5 T) et un système MR Signa HDx de GE (3 T) équipé de la version logicielle 15\LX\MR, édition 15.0.M4.0910.a.

L'artéfact d'image a été mesuré de manière non clinique dans un système RM Signa HDx de GE (3 T) conformément à la norme ASTM F2119-07, à l'aide d'un écho de spin et des séquences d'écho de gradient indiquées dans ce document. Les images d'écho de spin montraient des artéfacts clairs et foncés allant jusqu'à 40 mm de l'implant et bouchant la lumière de manière partielle à complète. Les images d'écho de gradient montraient des artéfacts opaques clairs et foncés et des artéfacts triangulaires foncés allant jusqu'à 40 mm de l'implant et bouchant la lumière de manière partielle à complète. Il est possible de procéder à une réduction dans l'artéfact à l'aide de séquences conçues pour réduire les artéfacts de métal.

12. Informations du patient

12.1 Carte d'identification de la recherche

Une carte d'identification de la recherche est donnée à chaque sujet sur qui a été implantée la bioprothèse aortique péricardique d'Edwards, modèle 11000A.

12.2 Documents d'informations du patient

Il est possible d'obtenir des documents d'informations du patient d'Edwards ou de l'un de ses spécialistes des ventes cliniques.

13. Références

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Ce produit est fabriqué et distribué selon au moins un des brevets américains suivants : Nos de brevets américains 5,928,281; 5,931,969; 5,961,549; 6,102,944; 6,245,105; 6,413,275; 6,561,970; 6,585,766; 6,837,902; 6,945,997; 7,214,344; 7,972,376; 8,007,992; 8,357,387; 8,366,769; 8,632,608; et RE 40570; ainsi que les brevets étrangers correspondants. De plus, des brevets supplémentaires sont en attente.

Se référer à la légende des symboles à la fin du document.

Tableau 2 - Récapitulation des taux de complications, modèle 2700

	Population ayant subi isolémentun RVA			Population ayant subi un RDV		
Complication	**Opératoires % de pt**	**Post Opératoires % par année-patient**	**% sans événement après 6 ans (écart-type)**	**Opératoires % de pt**	**Post Opératoires % par année-patient**	**% sans événement après 6 ans (écart-type)**
Décès	4,7	4,6	73,5 (2,0)	12,9	4,2	67,2 (6,5)
Explantation	0	0,3	98,5 (1,0)	0	0,8	S.O.*
Nouvelle opération en lien avec la valvule	0,7	0,1	99,8 (0,4)	0	0	S.O.*
Toutes les nouvelles opérations	22,4	1,8	75,4 (1,8)	34,3	2,3	S.O.*
Thrombo-embolie en lien avec la valvule	3,1	1,5	91,4 (1,1)	1,4	5,1	S.O.*
Toutes les thrombo-embolies	5,0	2,4	84,9 (1,6)	5,7	6,6	S.O.*
Endocardite	0,6	0,8	95,8 (0,9)	1,4	1,5	S.O.*
Dysfonction de la valvule	0,1	0,7	96,0 (1,1)	0	0,4	S.O.*
Fuite périvalvulaire	0,1	0,3	98,8 (0,5)	0	1,2	S.O.*
Complication hémorragique anticoagulation	1,4	0,4	96,4 (1,1)	4,3	2,3	S.O.*
Hémolyse	0	0,2	99,1 (0,4)	0	0,4	S.O.*
Thrombose de la valvule	0	0	100,0 (0)	0	0,4	S.O.*

* S.O. = sans objet

Tableau 3 - Résultats de l'échocardiographie postopératoire, modèle 2700

	Taille de la valvule						
	19 mm	**21 mm**	**23 mm**	**25 mm**	**27 mm**	**29 mm**	**Total**
Total N	12	22	15	8	3	3	63
Moyenne des mois après l'opération	28,6 ± 7,2	34,9 ± 8,6	36,9 ± 9,2	39,9 ± 7,6	31,4 ± 15,9	15,3 ± 12,2	34,6 ± 9,2
Vélocité (M/s)							
moyen ± E.-T.	2,80 ± 0,49	2,56 ± 0,46	2,36 ± 0,42	2,15 ± 0,56	2,09 ± 0,27	2,08 ± 0,1	2,46 ± 0,50
n =	12	21	15	7	3	3	61
Plage	1,90 - 3,60	1,90 - 3,90	1,39 - 2,86	1,00 - 2,60	1,90 - 2,40	2,05 - 2,10	1,00 - 3,90
Gradient instantané de crête (mmHg)							
moyen ± E.-T.	32,22 ± 11,08	27,04 ± 10,49	23,00 ± 7,30	19,50 ± 8,16	17,60 ± 4,70	14,4 ± 0,58	25,67 ± 10,14
n =	12	21	15	7	3	3	61
Plage	14,40 - 51,80	14,40 - 60,80	7,70 - 32,70	4,00 - 27,00	14,40 - 23,00	13,95 - 15,06	4,00 - 60,80

Tableau 4 - Résultats en matière d'efficacité, classification fonctionnelle de la NYHA, modèle 2700

Préopératoire Classification fonctionnelle de la NYHA	postopératoire Classification fonctionnelle de la NYHA					
	I	II	III	IV	Décès	Non disponible
I	18	19			9	
II	140	37			35	15
III	181	48	4	1	72	24
IV	43	16	2		53	2
Non disponible	5	1			2	2

Tableau 5 - Latitude concernant les taux de complications après 20 ans (N = 267), modèle 2700

Latitude concernant les taux de complications après 20 ans	Réelle	Actuarielle	Linéarisée (%/année-patient)
Décès en lien avec la valvule	85,8 ± 2,5%	67,9 ± 6,6%	1,2
Thrombo-embolie/thrombose	82,4 ± 2,6%	68,2 ± 6,8%	1,7
Saignement	94,0 ± 1,5%	91,7 ± 2,2%	0,4
Endocardite/sepsie	91,7 ± 1,7%	89,3 ± 2,4%	0,8
Explantation due à une DSV			
≥ 60	92,6 ± 2,0%	77,1 ± 7,2%	n.p.*
≥ 65	96,3 ± 1,6%	81,5 ± 9,6%	
> 70	96,0 ± 2,3%	69,9 ± 20,5%	

** Non pertinent. La DSV ne relève pas d'une fonction de risque constante. Par conséquent, les taux linéarisés ne sont pas significatifs.*

Tableau 6 - Résumé des événements indésirables en lien avec la valvule, modèles 3000 et 3000TFX

	≤ 30 jours après l'opération		> 30 jours après l'opération	
Événements indésirables	**3000TFX (N = 193) Nbre d'événements (% de patients)**	**3000/3000TFX (N = 253) Nbre d'événements (% de patients)**	**3000TFX (N = 193) Nbre d'événements (% de patients)**	**3000/3000TFX (N = 253) Nbre d'événements (% de patients)**
Thrombo-embolies en lien avec la valvule	6 (3,1)	7 (2,8)	3 (2,0)	3 (1,4)
Dysfonction non structurelle de la valvule (PVL)	3 (1,5)	4 (1,6)	3 (2,0)	3 (1,4)
Explantation (DNSV)	2 (1,0)	2 (0,8)	0 (0,0)	0 (0,0)
Décès (arrêt cardiaque, saignement, AVC)	1 (0,5)	1 (0,4)	3 (2,0)	3 (1,4)
Nouvelle opération chirurgicale	1 (0,5)	1 (0,4)	1 (0,7)	1 (0,5)
Hémolyse	1 (0,5)	1 (0,4)	3 (2,0)	3 (1,4)
Saignement en lien avec l'AC	0 (0,0)	0 (0,0)	2 (1,4)	2 (1,0)
Endocardite	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Détérioration de la structure de la valvule	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Thrombose de la valvule	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Autre (déchirure de l'aorte)	1 (0,5)	1 (0,4)	0 (0,0)	0 (0,0)

Tableau 7 - Variables hémodynamiques à l'évaluation échographique du suivi d'un an, modèles 3000 et 3000TFX

Type de valvule	Variable	19 mm Moyenne ± écart-type (N)	21 mm Moyenne ± écart-type (N)	23 mm Moyenne ± écart-type (N)	25 mm Moyenne ± écart-type (N)	27 mm Moyenne ± écart-type (N)	29 mm Moyenne ± écart-type (N)
3000TFX	Gradient systolique moyen (mmHg)	16,7 ± 4,7 (10)	15,8 ± 4,4 (18)	11,3 ± 3,7 (45)	11,1 ± 4,1 (37)	9,4 ± 4,3 (12)	9,0 ± 0,0 (2)
	Fraction d'éjection (%)	65,8 ± 10,4 (10)	62,7 ± 9,4 (19)	60,6 ± 11,3 (48)	61,4 ± 11,2 (38)	59,5 ± 10,7 (12)	55,0 ±14,1 (2)
	Aire valvulaire efficace de l'aorte (cm^2)	1,2 ± 0,4 (10)	1,5 ± 0,4 (18)	1,8 ± 0,6 (44)	1,8 ± 0,5 (36)	2,1 ± 0,6 (12)	2,1 ± 0,1 (2)
3000/ 3000TFX	Gradient systolique moyen (mmHg)	16,7 ± 4,2 (16)	13,8 ± 4,8 (34)	11,7 ± 4,7 (56)	11,0 ± 3,8 (47)	9,5 ± 4,1 (14)	9,0 ± 0,0 (2)
	Fraction d'éjection (%)	62,1 ± 15,1 (16)	58,6 ± 11,6 (34)	60,2 ± 11,2 (59)	60,2 ± 11,5 (47)	58,5 ± 10,5 (14)	55,0 ± 14,1 (2)
	Aire valvulaire efficace de l'aorte (cm^2)	1,3 ± 0,5 (16)	1,5 ± 0,4 (32)	1,8 ± 0,6 (55)	1,8 ± 0,6 (46)	2,1 ± 0,6 (14)	2,1 ± 0,1 (2)

Tableau 8 - Classe fonctionnelle de la NYHA : changement par rapport à l'évaluation de base lors de la visite de un an, modèles 3000 et 3000TFX

		-----Évaluation de base-----				
Type de valvule	**Suivi de la classification NYHA**	**Classe I**	**Classe II**	**Classe III**	**Classe IV**	**S.O.**
3000TFX N = 193	**Classe I**	10	33	51	10	3
	Classe II	2	8	13	2	1
	Classe III	-	-	3	-	-
	Classe IV	-	-	-	1	-
	Décès	-	3	16	1	-
	Explantation	-	-	3	-	-
	S.O.	2	6	21	4	-
3000/ 3000TFX N = 253	**Classe I**	12	40	71	11	3
	Classe II	2	14	29	3	1
	Classe III	-	-	3	-	-
	Classe IV	-	-	1	1	-
	Décès	-	3	19	2	-
	Explantation	-	-	3	-	-
	S.O.	2	7	22	4	-

Classe de fonctionnement de la NYHA : changement par rapport à l'évaluation de base lors de la visite de un an

Type de valvule	Amélioration N (%)	Identique N (%)	Aggravation N (%)	S.O. N (%)
3000TFX (N = 193)	109 (56,5)	22 (11,4)	2 (1,0)	60 (31,1)
3000/3000TFX (N = 253)	154 (60,9)	30 (11,9)	3 (1,2)	66 (26,1)

Polski

Osierdziowa bioproteza aortalna Edwards model 11000A

Instrukcja użytkowania

PRZESTROGA: Urządzenie badawcze. Prawo federalne. (Stanów Zjednoczonych Ameryki) ogranicza użytkowanie tego przyrządu do celów badawczych.

PRZESTROGA: Urządzenie badawcze. Wyłącznie do badań klinicznych.

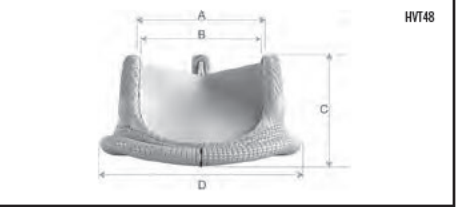
Przestroga: Urządzenie badawcze. Przeznaczone wyłącznie do celów badawczych. Do stosowania wyłącznie przez wykwalifikowanych badaczy (lekarzy).

1. Opis urządzenia i akcesoriów

1.1 Opis urządzenia

Osierdziowa bioproteza aortalna Edwards model 11000A jest trójpłatkową bioprotezą wykonaną z odpowiednio przygotowanego wołowego osierdzia, umocowaną na elastycznej ramie. Bioproteza jest dostępna w rozmiarach 19, 21, 23, 25, 27 i 29 mm (tabela 1). Bioproteza jest przechowywana w opakowaniu niewodnym i nie wymaga przemywania przed wszczepieniem.

Tabela 1. Nominalne wymiary



Rozmiar	19 mm	21 mm	23 mm	25 mm	27 mm	29 mm
A. Średnica pierścienia tkanki (średnica stentu, mm)	19	21	23	25	27	29
B. Średnica wewnętrzna (średnica wewnętrzna stentu, mm)	18	20	22	24	26	28
C. Wysokość profilu (mm)	13	14	15	16	17	18
D. Zewnętrzna średnica pierścienia do wszywania (mm)	24	26	28	30	32	34
Powierzchnia geometryczna otworu (mm^2)	235	289	354	420	499	570

Prowadnica druciana jest wykonana ze stopu kobaltowo-chromowego i jest pokryta tkaniną poliestrową. Stop kobaltowo-chromowy/warstwa laminatu poliestrowego otacza podstawę ramy prowadnicy drucianej.

Silikonowy pierścień do wszywania pokryty porowatym politetrafluoroetylenem (PTFE) jest przymocowany do ramy prowadnicy drucianej. Pierścień do wszywania ma trzy czarne jedwabne oznaczenia szwów rozmieszczone w równych odległościach w środku zastawki w celu ułatwienia ustawienia bioprotezy i założenia szwów.

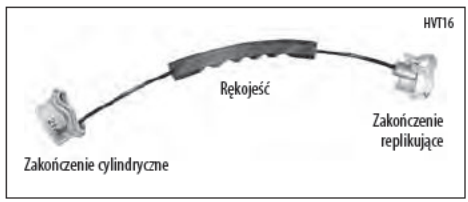
Uchwyt jest dołączony do bioprotezy za pomocą szwów w celu ułatwienia obchodzenia się z bioprotezą i jej wszycia w trakcie implantacji. Uchwyt może zostać łatwo odłączony przez chirurga. (Patrz **10.4 Implantacja urządzenia**)

1.2 Opis akcesoriów

Kalibratory i taca

Zastosowanie kalibratora ułatwia wybór prawidłowego rozmiaru bioprotezy do implantacji. Półprzezroczysty model kalibratorów 1133 umożliwia bezpośrednią obserwację ich dopasowania w obrębie pierścienia. Każdy kalibrator składa się z rękojeści z różną konfiguracją narzędzi pomiarowych na każdym zakończeniu (Rysunek 1a). Na jednym końcu rękojeści znajduje się zakończenie cylindryczne z wchodzącą w jego skład krawędzią, która odzwierciedla geometrię pierścienia do wszywania bioprotezy (Rysunek 1b). Na jej drugim końcu znajduje się zakończenie replikujące bioprotezy, które odzwierciedla zarówno geometrię pierścienia do wszywania, jak i wysokość oraz lokalizację wsporników stentu (Rysunek 1c). Kalibrator jest dostępny dla każdego rozmiaru bioprotezy model 11000A (19, 21, 23, 25, 27 i 29 mm). Kompletny zestaw kalibratorów jest umieszczony na tacy model TRAY1133, która może zostać ponownie wykorzystana i wysterylizowana.

Rysunek 1a. Kalibrator aortalny



Rysunek 1b. Zakończenie cylindryczne

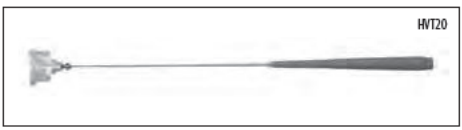
Rysunek 1c. Zakończenie replikujące

Uchwyt i rękojeść bioprotezy

Zespół uchwyt/rękojeść składa się z dwóch części: integralnej, jednorazowej części, fizycznie przymocowanej do bioprotezy przez producenta oraz giętkiej rękojeści (model 1111 do wielokrotnego użytku lub jednorazowy model 1126), dołączanej do uchwytu w czasie operacji (Rysunki 2a i 2b).

Rysunek 2a. Rękojeść model 1111

Rysunek 2b. Rękojeść model 1126



2. Wskazania do stosowania

Osierdziowa bioproteza aortalna Edwards model 11000A jest przeznaczona dla pacjentów wymagających wymiany naturalnej lub protetycznej zastawki aortalnej.

3. Przeciwwskazania

Nie stosować bioprotezy, jeżeli chirurg uzna jej użycie za sprzeczne z najlepiej pojętym interesem pacjenta. To chirurg powinien podjąć decyzję dotyczącą zastosowania tej bioprotezy lub zrezygnowania z jej użycia, ponieważ może ocenić różne czynniki ryzyka związane z jej wszczepieniem, w tym również budowę anatomiczną pacjenta oraz zmiany patologiczne widoczne podczas operacji.

4. Ostrzeżenia

WYŁĄCZNIE DO JEDNORAZOWEGO UŻYTKU. Opisywane urządzenie jest zaprojektowane i rozprowadzane wyłącznie z zamiarem jednorazowego użytku i takie jest jego przeznaczenie. Niniejszego produktu nie wolno ponownie sterylizować/używać. Nie istnieją żadne dane potwierdzające jałowość, niepirogenność i sprawność produktu po ponownej sterylizacji.

NIE WOLNO ZAMRAŻAĆ BIOPROTEZY ANI PODDAWAĆ DZIAŁANIU SKRAJNIE WYSOKIEJ TEMPERATURY. Narażenie bioprotezy na skrajne temperatury uczyni urządzenie niezdatnym do użycia.

Protezy biologicznej NIE NALEŻY UŻYWAĆ:

- **jeśli torebka foliowa, zapieczętowane tace lub pokrywy są otwarte, uszkodzone lub zabrudzone**
- **jeśli minął termin ważności lub**
- **jeśli bioproteza została upuszczona, zniszczona lub postępowano z nią w niewłaściwy sposób. Jeśli podczas wszczepiania bioproteza ulegnie uszkodzeniu, nie należy podejmować próby jej naprawy.**

NIE NALEŻY NARAŻAĆ bioprotezy na działanie jakichkolwiek roztworów, środków chemicznych, antybiotyków itp., z wyjątkiem jałowego roztworu soli fizjologicznej. Może nastąpić nienaprawialne uszkodzenie tkanki płatków, które może nie być widoczne gołym okiem.

NIE WOLNO CHWYTAĆ tkanki płatków bioprotezy narzędziami ani w żaden sposób uszkadzać bioprotezy. Nawet najmniejsza perforacja tkanki płatków może z czasem ulec powiększeniu, powodując znaczne upośledzenie czynności bioprotezy.

NIE NALEŻY STOSOWAĆ ZBYT DUŻEGO ROZMIARU. Stosowanie zbyt dużego rozmiaru może spowodować uszkodzenie bioprotezy lub miejscowe naprężenia mechaniczne, których efektem może być zranienie serca, zniszczenie tkanki płatków, zniekształcenie stentu i przepływ fali zwrotnej.

Podobnie jak w przypadku każdego implantowanego przyrządu medycznego, istnieje ryzyko odpowiedzi immunologicznej u pacjenta. Do składników modelu 11000A należy stop metalu, który zawiera kobalt, chrom, nikiel, molibden, mangan, węgiel, beryl oraz żelazo. Należy zachować ostrożność u pacjentów z nadwrażliwościami na te materiały. Urządzenie zostało wytworzone bez lateksu, ale mogło być produkowane w środowisku zawierającym lateks.

5. Zdarzenia niepożądane

5.1 Zaobserwowane zdarzenia niepożądane

Podobnie jak w przypadku wszystkich sztucznych zastawek serca, stosowanie zastawek tkankowych może wiązać się z poważnymi zdarzeniami niepożądanymi, niekiedy prowadzącymi do zgonu. Ponadto po upływie różnych okresów czasu (godzin lub dni) mogą występować zdarzenia niepożądane wynikające z indywidualnej reakcji pacjenta na wszczepione urządzenie lub fizycznych i chemicznych zmian jego komponentów, zwłaszcza pochodzenia biologicznego; mogą one powodować konieczność ponownej operacji i wymiany protezy.

Osierdziowa bioproteza aortalna Edwards model 11000A jest podobna w konstrukcji do bioprotez osierdziowych Carpentier-Edwards PERIMOUNT Magna Ease model 3300TFX.

Do zdarzeń niepożądanych związanych z zastosowaniem bioprotez osierdziowych Carpentier-Edwards PERIMOUNT według zestawienia na podstawie źródeł literaturowych i doniesień otrzymanych z systemu nadzoru nad produktem, zgodnie z przepisami prawa federalnego USA ustalającymi dobrą praktykę produkcyjną, rozdział 820.198, zalicza się: zwężenie, niedomykalność niewydolnej zastawki, nieszczelność wokół zastawki, zapalenie wsierdzia, hemolizę, zaburzenia zakrzepowo-zatorowe, zaburzenia przepływu spowodowane przez zakrzep, skazy krwotoczne związane z leczeniem przeciwzakrzepowym, a także wadliwe funkcjonowanie zastawki wskutek zniekształcenia implantu, złamania prowadnicy drucianej albo zmian fizycznych lub chemicznych komponentów zastawki. Do rodzajów uszkodzenia tkankowego należy zakażenie, zwapnienie, pogrubienie, perforacja, degeneracja, przetarcie szwu, uraz narzędziem oraz odłączenie płatka od wsporników stentu zastawki. Manifestacją kliniczną tych powikłań mogą być nieprawidłowe szmery serca, duszności, nietolerancja wysiłku, duszność, ortopnoe, niedokrwistość, gorączka, arytmia, krwotok, przejściowe ataki niedokrwienne, udar mózgu, niedowład, niska pojemność minutowa serca, obrzęk płuc, zastoinowa niewydolność serca, niewydolność serca i zawał mięśnia sercowego.

Uwaga: Na podstawie doniesień w piśmiennictwie na temat zastawek tkankowych (poz. 6, 7, 8, 9 i 10) wydaje się występować zwiększony odsetek zwapnienia listków u pacjentów w wieku poniżej 20 lat. Badania na zwierzętach prowadzone w tym zakresie (poz. 11) wykazują, że wysoki poziom wapnia w krążeniu ustrojowym może prowadzić do wczesnego wapnienia. Ponadto przynajmniej jedno z opublikowanych doniesień opisuje potencjalną zależność pomiędzy codziennym spożywaniem preparatów wapnia i wczesnym wapnieniem płatków zastawek u osób dorosłych (poz. 13). Jeśli jest to możliwe, należy unikać powtarzanych dożylnych wstrzyknięć preparatów zawierających wapń w okresie pooperacyjnym, a dzieci powinny także unikać nadmiernego spożycia mleka oraz nabiału. Brak danych klinicznych wskazujących na zwiększoną odporność osierdziowej bioprotezy aortalnej Edwards model 11000A na zwapnienie w porównaniu do innych dostępnych na rynku bioprotez.

5.2 Możliwe zdarzenia niepożądane

Zdarzenia niepożądane potencjalnie związane z zastosowaniem bioprotez zastawek serca to:

- Dławica piersiowa
- Skazy krwotoczne związane z leczeniem przeciwzakrzepowym (koagulopatia)
- Zaburzenia rytmu serca

- Zablokowanie ujścia wieńcowego
- Zapalenie wsierdzia
- Niewydolność serca
- Hemoliza
- Niedokrwistość hemolityczna
- Krwotok
- Miejscowe i/lub uogólnione zakażenie
- Zawał mięśnia sercowego
- Niedopasowanie protezy do pacjenta (PPM)
- Usidlenie płatka zastawki (wklinowanie)
- Niestrukturalna dysfunkcja protezy
- Wytworzenie łuszczki
- Przeciek okołozastawkowy
- Niedomykalność protezy
- Strukturalne uszkodzenie protezy
- Zakrzepica protezy
- Udar mózgu
- Zaburzenia zakrzepowo-zatorowe
- Przemijające niedokrwienie mózgu (TIA)

Wymienione powikłania mogą prowadzić do:

- powtórnego zabiegu operacyjnego
- usunięcia zastawki
- trwałej niepełnosprawności
- zgonu

6. Badania kliniczne

Kohorta pacjentów przed zatwierdzeniem produktu

Dostępne dane kliniczne 719 pacjentów wymagających operacji wymiany jednej zastawki aortalnej (aortic valve replacement, AVR) na model bioprotezy osierdziowej 2700 Carpentier-Edwards PERIMOUNT, ze średnim okresem obserwacji wynoszącym 3,9 roku, wskazują na ogólny aktuarialny wskaźnik przeżycia 73,7% ± 2,0% w okresie 6 lat. Dostępne dane kliniczne 70 pacjentów wymagających operacji wymiany dwóch zastawek (double valve replacement, DVR), ze średnim okresem obserwacji wynoszącym 3,7 roku, wskazują na ogólny aktuarialny wskaźnik przeżycia 67,2% ± 6,5% w okresie 6 lat. Te dane dla grupy kontrolnej pacjentów przed zatwierdzeniem produktu zgromadzono w okresie od sierpnia 1981 do stycznia 1989 roku.

W populacji wymagającej pojedynczego zabiegu AVR znajdowało się ogółem 455 mężczyzn (63,3%) i 264 kobiety (36,7%), zaś średni wiek pacjentów podczas wszczepienia (± odchylenie standardowe) wynosił 64 lata (± 12,4) przy zakresie wieku od 18 do 90 lat. Wskazaniami do wymiany zastawki były zwężenie (63,4%), niedomykalność (16,3%), wada mieszana (15,3%) oraz dysfunkcja poprzedniej prostetycznej zastawki aortalnej (5,0%).

W populacji wymagającej zabiegu DVR znajdowało się ogółem 24 mężczyzn (34,3%) i 46 kobiet (65,7%), zaś średni wiek pacjentów podczas wszczepienia (± odchylenie standardowe) wynosił 62,9 lat (± 12,7) przy zakresie wieku od 31 do 94 lat. Wskazaniami do wymiany zastawki były: zwężenie (45,7%), niedomykalność (25,7%), wada mieszana (21,4%) oraz dysfunkcja poprzedniej protezy zastawki aorty (7,4%).

Metody obserwacji obejmowały wizyty w szpitalu, wizyty w gabinetach oraz kontakt telefoniczny lub listowny z pacjentem, jego rodziną lub miejscowym lekarzem.

Tabela 2 zawiera zestawienie współczynników powikłań operacyjnych i pooperacyjnych dla izolowanych populacji AVR i DVR. Obliczenia wskaźników z okresu operacji oparto na grupie 719 pacjentów przechodzących zabieg AVR i 70 pacjentów w grupie poddanej zabiegowi DVR. Wskaźniki pooperacyjne obliczono na podstawie obserwacji wynoszącej 2767,9 i 255,8 pacjentolat, odpowiednio dla grup poddanych zabiegom AVR i DVR, mającej miejsce > 30 dni po implantacji.

Tabela 3 przedstawia, według rozmiaru zastawki, wyniki echokardiografii w okresie pooperacyjnym dla tej populacji badania.

Zebrano informacje dotyczące przynależności pacjentów poddanych zabiegowi izolowanej AVR do poszczególnych klas czynnościowych NYHA przed i po operacji. Klasy czynnościowej NYHA nie podawano w przypadku 220 pacjentów (171 pacjentów zmarło, a 49 pacjentów nie było dostępnych). Spośród 499 pacjentów, u których podano klasę czynnościową NYHA przed i po operacji (z ostatniej dostępnej wizyty kontrolnej), 10 pacjentów (2,0%) wykazywało pogorszenie, stan 59 pacjentów (11,8%) pozostawał bez zmian, zaś u 430 pacjentów (86,2%) stwierdzono poprawę.

W tabeli 4 przedstawiono dane wynikające z porównania klasy czynnościowej NYHA sprzed operacji i po operacji z ostatniej wizyty kontrolnej.

Kohorta pacjentów po zatwierdzeniu produktu

Firma Edwards od listopada 1981 r. kontynuuje badania kontrolne zatwierdzonej kohorty 267 pacjentów, którzy przeszli zabieg wymiany wyłącznie jednej zastawki (AVR) (model 2700) z czterech ośrodków z oryginalnego badania klinicznego nad osierdziową bioprotezą Carpentier-Edwards PERIMOUNT. Ta grupa składa się ze 171 (64%) mężczyzn i 96 (36%) kobiet. Średni wiek tych pacjentów w chwili implantacji (± odchylenie standardowe) wynosił 64,9 ± 11,8 roku przy zakresie wieku od 21 do 86 lat. Łączna liczba danych w ilości 2407 pacjentolat była dostępna do analizy (2386 późnych pacjentolat). Średni czas obserwacji kontrolnej wynosił 9,0 ± 5,5 lat, a maksymalnie 20,3 lat. W okresie od 1981 r. do 1994 r. doszło łącznie do 189 zgonów. Czterdzieści osiem (25,3%) z tych 189 zgonów zostało uznane za powiązane z zastawkami. Metody obserwacji wykorzystywane w każdej klinice obejmowały wizyty w szpitalu, wizyty w gabinetach oraz kontakt telefoniczny lub listowny z pacjentem, jego rodziną lub miejscowym lekarzem.

Tabela 5 podsumowuje współczynniki wolności od powikłań po 20 latach. Stan pacjentów na ostatni okres obserwacji to 189 osób zmarłych (70,8%), 10 osób żyjących (3,8%), 46 osób poddanych zabiegowi usunięcia zastawki (17,2%) i 22 osoby, z którymi utracono kontakt podczas okresu obserwacji (8,2%).

W tej grupie pacjentów odnotowano 48 zgonów powiązanych z zastawką; do 1 zgonu powiązanego z zastawką doszło w okresie operacyjnym i wynikał on z krwawienia. Do dwudziestu ośmiu zgonów związanych z zastawką w okresie pooperacyjnym zaliczono 5 spowodowanych zaburzeniami zakrzepowo-zatorowymi, 4 spowodowane zapaleniem wsierdzia/posocznicą, 3 spowodowane strukturalnym uszkodzeniem protezy i 1 spowodowany krwawieniem. Wystąpiło 15 innych zgonów, które rozpatrywano jako związane z zastawką ze względu na brak danych lub w związku z tym, że zgon został zaklasyfikowany jako powiązany z zastawką przez badacza. Wolność aktuarialna od zgonu powiązanego z zastawką wynosiła 67,9 ± 6,6% po 20 latach. Dziewiętnaście dodatkowych zgonów były spowodowanych nieznanymi przyczynami lub nagłą śmiercią i mogło mieć związek z zastawką. Te zgony zaklasyfikowano w sposób zachowawczy jako powiązane z zastawką; odpowiednio, wynikająca aktuarialna wolność od zgonu powiązanego z zastawką wynosiła 55,4 ± 6,4% po 20 latach.

Wykazano także poprawę klasy czynnościowej NYHA w okresie pooperacyjnym. Zgodnie z ostatnimi wynikami obserwacji 108 pacjentów (44,8%) znajdowało się w I klasie czynnościowej NYHA.

Niniejsze dane zostały skompilowane na podstawie wieloośrodkowego badania klinicznego prowadzonego przez firmę Edwards Lifesciences. W celu uzyskania dodatkowych informacji na temat tego badania należy skontaktować się z Edwards Lifesciences LLC, Heart Valve Therapy Marketing Department, One Edwards Way, Irvine, CA 92614-5686.

Badanie potwierdzające

W okresie od sierpnia 2003 r. do stycznia 2004 r. 60 pacjentom z pięciu ośrodków (dwóch europejskich i trzech kanadyjskich), wymagającym wymiany zastawki aortalnej (AVR) wszczepiono bioprotezę aortalną Carpentier-Edwards PERIMOUNT Magna, model 3000. Wkrótce potem wprowadzono do protokołu klinicznego poprawki pozwalające na implantację bioprotezy aortalnej Carpentier-Edwards PERIMOUNT Magna, model 3000TFX, oraz dodanie trzech ośrodków amerykańskich. Następnie, w okresie od grudnia 2004 r. do grudnia 2006 r., 193 dodatkowym pacjentom wszczepiono model 3000TFX. Model 3000TFX różni się od modelu 3000 tym, że model 3000TFX jest poddawany procesowi ThermaFix.

W grupie modelu 3000TFX znajdowało się łącznie 116 mężczyzn (60,1%) i 77 kobiet (39,9%) o średniej wieku w momencie wszczepienia rzędu 72,0 (± 8,59 SD) lat i zakresie wieku od 26 do 89 lat. Głównym wskazaniem do wymiany zastawki było zwężenie (78,2%), a w dalszej kolejności wada mieszana (14,5%) oraz niedomykalność (7,3%).

W połączonej grupie modeli 3000 i 3000TFX znajdowało się łącznie 150 mężczyzn (59,3%) i 103 kobiety (40,7%) o średniej wieku w momencie wszczepienia rzędu 72,2 (± 8,31 SD) lata i zakresie wieku od 26 do 89 lat. Ponownie głównym wskazaniem do wymiany zastawki było zwężenie (77,5%), wada mieszana (15,4%) oraz niedomykalność (7,1%).

Stan pacjentów oceniano przedoperacyjnie, śródoperacyjnie, przy wypisywaniu ze szpitala, po 3 do 6 miesiącach, po 1 roku i następnie corocznie. Skumulowana obserwacja dla modelu 3000TFX wynosiła 167 pacjentolat, ze średnim okresem obserwacji wynoszącym 0,9 roku (SD = 0,42, zakres = 0,0 do 2,1 roku); a skumulowana obserwacja dla obu modeli 3000 i 3000TFX łącznie wynosiła 232 pacjentolat ze średnim okresem obserwacji wynoszącym 0,9 roku (SD = 0,42, zakres = 0,0 do 2,1 roku).

Tabela 6 podsumowuje wczesne (≤ 30 dni) oraz późne pooperacyjne (> 30 dni) współczynniki zdarzeń niepożądanych związanych z zastawką dla, odpowiednio, grup modelu 3000TFX i połączonych modeli 3000/3000TFX.

Ta bela 7 ilustruje, według modelu zastawki, zmienne hemodynamiczne odnotowywane w elektrokardiogramach po jednym roku, wykonywanych na pacjentach w badaniach modelu 3000TFX i połączonych modeli 3000/3000TFX.

Tabela 8 prezentuję zmianę w klasie czynnościowej NYHA od oceny dokonywanej w momencie wyjściowym do wizyty po 1 roku. Należy zwrócić uwagę na fakt, że w przypadku modelu 3000TFX odnotowano poprawę klasy czynnościowej na poziomie 56,5% dla wizyty po 1 roku. Dla modelu grupy łączonej 3000/3000TFX odnotowano 60,9% poprawę klasy czynnościowej dla wizyty po 1 roku.

Kilka opublikowanych badań klinicznych demonstruje długoterminową trwałość osierdziowych bioprotez aortalnych Carpentier-Edwards PERIMOUNT, na podstawie których konstruowano osierdziowe bioprotezy aortalne Carpentier-Edwards PERIMOUNT Magna oraz Magna Ease (poz. 14, 15, 16 & 17). Ponadto opublikowane dane pokazują, że bioproteza aortalna PERIMOUNT Magna wykazuje wyjątkowe parametry hemodynamiczne, z bardzo niskim ryzykiem niedopasowania pacjenta i protezy (poz. 18, 19, 20, 21, 22 & 23).

7. Indywidualizacja leczenia

We wszystkich przypadkach bez przeciwwskazań pacjenci z wszczepionymi bioprotezami zastawek serca powinni otrzymywać leczenie przeciwzakrzepowe podczas wstępnych etapów po implantacji indywidualnie, według zaleceń lekarza. Długoterminowe leczenie przeciwzakrzepowe i/lub przeciwpłytkowe należy rozważyć u pacjentów z czynnikami ryzyka zaburzeń zakrzepowo-zatorowych.

Ostateczną decyzję w sprawie opieki nad konkretnym pacjentem powinien podjąć personel medyczny oraz pacjent, w świetle wszystkich okoliczności dotyczących tego pacjenta (poz. 12). Bioproteza jest zalecana do AVR u pacjentów w każdym wieku, którzy nie będą przyjmować warfaryny lub mają poważne przeciwwskazania medyczne do leczenia warfaryną. Preferencje pacjenta to racjonalne kryterium przy wyborze operacji wymiany zastawki aortalnej oraz wyborze protezy aortalnej. Mechaniczna bioproteza jest rozsądnym wyborem do AVR u pacjentów poniżej 65 roku życia, którzy nie mają przeciwwskazania do leczenia przeciwzakrzepowego. Bioproteza jest rozsądnym wyborem do AVR u pacjentów poniżej 65 roku życia, którzy wybrali wymianę zastawki ze względów związanych ze stylem życia po szczegółowych omówieniach ryzyka leczenia przeciwzakrzepowego względem prawdopodobieństwa konieczności przeprowadzenia kolejnego zabiegu AVR (poz. 12).

7.1 Szczególne grupy pacjentów

Nie potwierdzono bezpieczeństwa ani skuteczności stosowania modelu bioprotez 11000A w następujących szczególnych populacjach, ponieważ nie przebadano ich w takich grupach:

- kobiety ciężarne;
- matki karmiące;
- pacjenci z nieprawidłowym metabolizmem wapnia (np. z przewlekłą niewydolnością nerek lub nadczynnością przytarczyc);
- pacjenci ze schorzeniami zwyrodnieniowymi aorty powodującymi powstawanie tętniaków (np. martwica torbielowata błony środkowej, zespół Marfana);
- dzieci, młodzież lub młode osoby dorosłe.

Przestroga: Na podstawie doniesień w piśmiennictwie na temat zastawek tkankowych (poz. 6, 7, 8, 9 i 10) wydaje się występować zwiększony odsetek zwapnienia listków u pacjentów w wieku poniżej 20 lat. W miarę możliwości należy unikać podawania w okresie pooperacyjnym wielokrotnych wstrzyknięć dożylnych zawierających wapń oraz unikać spożywania przez dzieci nadmiernych ilości mleka lub nabiału. Wyniki badań prowadzonych na zwierzętach (poz. 11) wskazują, że wysoki poziom wapnia w organizmie może prowadzić do wczesnego powstawania zwapnień.

8. Informacja dla pacjenta

Po operacji zaleca się uważną i stałą obserwację lekarską (przynajmniej jedna wizyta rocznie), aby umożliwić rozpoznanie i właściwe leczenie powikłań związanych z bioprotezą, szczególnie wynikających z uszkodzenia materiału. Pacjentom z bioprotezą, którzy są w grupie podwyższonego ryzyka bakteriemii (np. poddawanym zabiegom stomatologicznym), warto doradzić profilaktyczną terapię antybiotykową. Pacjentom należy doradzać, aby zawsze nosili przy sobie Kartę danych wszczepu oraz informowali pracowników służby zdrowia o posiadanym implancie przy zasięganiu porady lekarskiej.

9. Sposób dostarczania

9.1 Opakowanie

Osierdziowa bioproteza aortalna Edwards model 11000A jest dostarczana w postaci jałowej i niepirogennej w opakowaniu tacowym z podwójną ochroną. Opakowanie tacowe z podwójną ochroną mieści się w torebce foliowej, która znajduje się w kartonie.

Każda bioproteza umieszczona jest w kartonie ze wskaźnikiem temperatury widocznym przez okienko na panelu bocznym. Wskaźnik temperatury przeznaczony jest do identyfikacji produktów narażonych na przejściowe skrajne warunki temperaturowe. W chwili otrzymania bioprotezy należy niezwłocznie sprawdzić wskaźnik i zapoznać się z etykietą kartonu, aby potwierdzić stan „Do wykorzystania". Jeśli stan „Do wykorzystania" nie jest oczywisty, nie należy używać bioprotezy i skontaktować się z lokalnym dostawcą lub przedstawicielem firmy Edwards Lifesciences w celu dokonania ustaleń dotyczących potwierdzenia zwrotu i wymiany.

Ostrzeżenie: Dokładnie sprawdzić bioprotezę przed implantacją pod kątem dowodów ekspozycji na skrajne temperatury lub innych uszkodzeń.

9.2 Przechowywanie

Osierdziową bioprotezę aortalną Edwards model 11000A należy przechowywać w temperaturze 10°C do 25°C (50-77°F), w torebce foliowej i na półce kartonowej.

10. Wskazówki dotyczące użycia

10.1 Szkolenia lekarzy

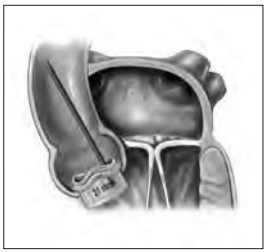
Techniki implantacji niniejszej bioprotezy są podobne do stosowanych podczas wszczepiania ponad pierścieniem jakichkolwiek stentowych protez biologicznych zastawki aorty. Przeszkolenie lekarzy nie jest konieczne do wykonywania implantacji osierdziowej bioprotezy aortalnej Edwards model 11000A.

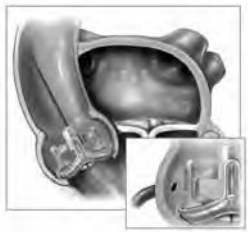
10.2 Kalibrowanie

Sprawdzić, czy akcesoria zostały wyjałowione zgodnie z zalecanymi instrukcjami dostarczonymi z akcesoriami wielorazowymi.

Kalibrowanie w implantacji nadpierścieniowej

W celu przeprowadzenia implantacji nadpierścieniowej pierścień do wszywania bioprotezy należy umieścić nad pierścieniem włóknistym, maksymalnie powiększając w ten sposób otwór zastawki. Podczas dobierania rozmiaru do implantacji nadpierścieniowej kalibrator powinien być ułożony równolegle do płaszczyzny pierścienia; należy zastosować następującą technikę kalibracji:

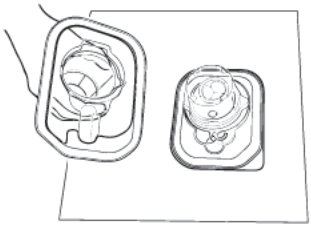
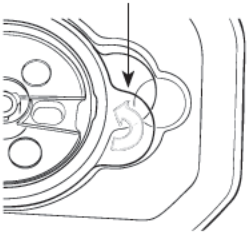
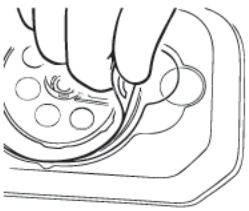
Krok	Postępowanie
1	Używając kalibratora model 1133, wybrać cylindryczne zakończenie kalibratora o największej średnicy, które można bez trudu dopasować do pierścienia włóknistego pacjenta. HVT21 

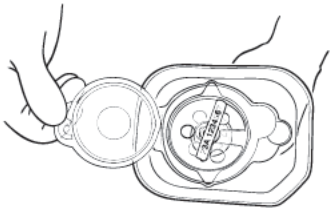
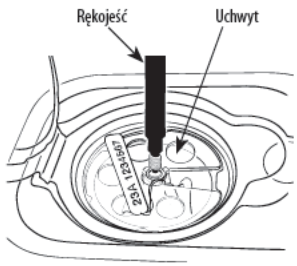
Krok	Postępowanie
2	Po zweryfikowaniu odpowiedniego zakończenia cylindrycznego należy użyć zakończenia replikującego w tym samym rozmiarze, aby sprawdzić, czy pierścień do wszywania będzie dobrze dopasowany do górnej części pierścienia włóknistego. Należy zwrócić szczególną uwagę na to, czy ujścia naczyń wieńcowych nie są zablokowane i czy wsporniki stentu zakończenia replikującego nie kolidują ze ścianą aorty przy połączeniu opuszkowo-komorowym. Jeśli dopasowanie zakończenia replikującego jest satysfakcjonujące, do implantacji należy wybrać ten rozmiar bioprotezy. HVT37 

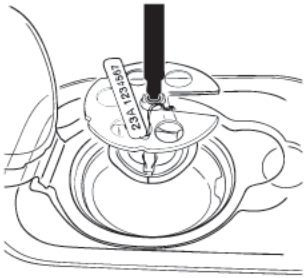
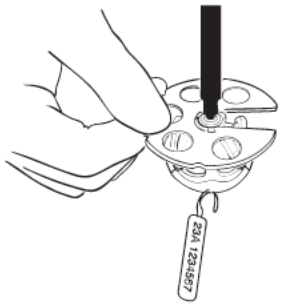
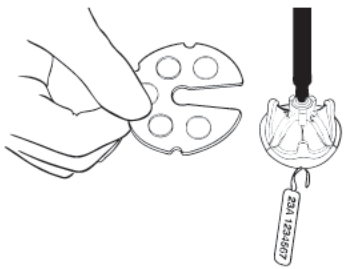
10.3 Instrukcje dotyczące manipulacji i przygotowania

Zaleca się przeprowadzenie szkolenia w miejscu pracy przed rozpoczęciem manipulowania i przygotowania osierdziowej bioprotezy aortalnej Edwards, model 11000A.

Krok	Postępowanie
1	**Przestroga: Nie otwierać opakowania osierdziowej bioprotezy aortalnej Edwards, model 11000A przed upewnieniem się, że dojdzie do implantacji.** **Ostrzeżenie: Nie otwierać torebki foliowej w polu jałowym. Torebka foliowa stanowi jedynie osłonę zabezpieczającą. Jedynie najbardziej wewnętrzne opakowanie tacowe można wprowadzać do pola jałowego.** Po wyborze odpowiedniego rozmiaru bioprotezy należy, poza polem jałowym, wyjąć z kartonu torebkę foliową. Przed otwarciem należy sprawdzić, czy opakowanie nie jest uszkodzone i czy nie brakuje pieczęci lub czy nie są one uszkodzone.
2	Należy przytrzymać podstawę tacy zewnętrznej w pobliżu pola jałowego i oderwać pokrywę tacy zewnętrznej.

Krok	Postępowanie
3	Taca wewnętrzna i jej zawartość są jałowe. Należy przełożyć tacę wewnętrzną do pola jałowego. Przy postępowaniu z wewnętrzną tacą należy stosować jałowe techniki chirurgiczne w celu uniknięcia skażenia. HVT26 
4	**Przestroga: Nie otwierać wewnętrznego opakowania przed upewnieniem się, że dojdzie do implantacji, i zanim chirurg nie przygotuje się do umieszczenia zastawki.** **Przestroga: Bioproteza nie jest przymocowana do tacy wewnętrznej. Należy ostrożnie odrywać pokrywę i otwierać plastikowy języczek.** Przed otwarciem należy sprawdzić, czy taca i pokrywa nie są uszkodzone i czy nie brakuje pieczęci lub czy nie są one uszkodzone. Należy przytrzymać podstawę tacy wewnętrznej w pobliżu pola sterylnego i oderwać pokrywę tacy wewnętrznej.
5	W celu uzyskania dostępu do bioprotezy należy pociągnąć w górę plastikowy języczek ze strzałką. HVT28 Pociągnąć za języczek ze strzałką  HVT29 

Krok	Postępowanie
	HVT30 
6	Przed wyjęciem bioprotezy z tacy należy przymocować rękojeść model 1111 lub model 1126 do uchwytu bioprotezy. W celu połączenia należy włożyć rękojeść do uchwytu i obracać zgodnie z ruchem wskazówek zegara do momentu napotkania oporu. **Przestroga: Bioprotezy nie należy chwytać rękoma ani za pomocą narzędzi chirurgicznych.** **Przestroga: Nie należy wypychać bioprotezy z zaczepu podczas mocowania rękojeści do uchwytu.** **Przestroga: Zespół rękojeść/uchwyt jest potrzebny w trakcie implantacji i nie należy go usuwać do momentu przyszycia bioprotezy do pierścienia.** **Przestroga: Należy zwrócić uwagę, by w trakcie mocowania nie dopuścić do zaplątania etykiety z numerem seryjnym wokół rękojeści.** HVT31 

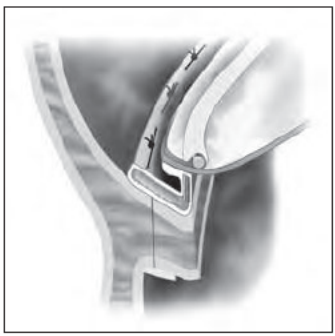
Krok	Postępowanie
7	Po przymocowaniu rękojeści należy usunąć bioprotezę i zaczep z tacy wewnętrznej. HVT32 
8	W celu usunięcia zaczepu z bioprotezy należy chwycić zaczep i odciągnąć go od zespołu rękojeść/uchwyt. HVT33  HVT34 

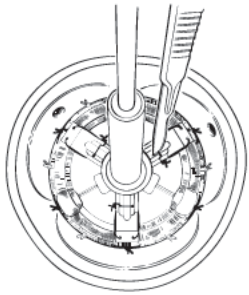
Krok	Postępowanie
9	Do każdego pierścienia do wszywania protezy biologicznej dołączona jest etykieta z numerem seryjnym. Należy sprawdzić, czy numer seryjny jest zgodny z numerem na opakowaniu bioprotezy i kartą danych implantacji bioprotezy. Etykiety nie należy odrywać od bioprotezy przed upewnieniem się, że dojdzie do wszczepienia. **Przestroga: W przypadku zauważenia jakiejkolwiek różnicy w numerze seryjnym należy zwrócić nieużywaną bioprotezę.** **Przestroga: Należy zwrócić szczególną uwagę na to, aby podczas usuwania etykiety z numerem seryjnym uniknąć nacięcia lub rozerwania tkaniny pierścienia do wszywania.** **Przestroga: By uniknąć uszkodzenia tkaniny pierścienia do wszywania, nie należy przeciągać supła szwu z etykietą z numerem seryjnym przez pierścień do wszywania.**
10	Osierdziowa bioproteza aortalna Edwards model 11000A **NIE WYMAGA PŁUKANIA** przed implantacją. **Przestroga: Jeśli bioproteza zostanie wypłukana przed implantacją, należy ją utrzymywać w stanie nawodnienia jałowym roztworem soli fizjologicznej po obu stronach tkanki płatka przez pozostały czas trwania zabiegu chirurgicznego. Zaleca się przepłukiwanie co 1 lub 2 minuty.** **Przestroga: Należy unikać kontaktu tkanki płatka z ręcznikami, płótnem i innymi źródłami materii pylastej, która może zostać przeniesiona na tkankę płatka.**

10.4 Implantacja urządzenia

Osierdziowa bioproteza aortalna Edwards model 11000A jest przeznaczona do implantacji nadpierścieniowej.

Krok	Postępowanie
1	Chirurg powinien znać zalecenia dotyczące doboru rozmiarów oraz umiejscowienia protezy ponad pierścieniem (Patrz **10.2 Kalibrowanie**). Ze względu na złożoność i rodzaje operacji wymiany zastawki serca, wybór techniki chirurgicznej, odpowiednio zmodyfikowanej zgodnie z wcześniej opisanymi **Ostrzeżeniami**, zależy od decyzji chirurga. Zasadniczo należy wykonać następujące kroki: 1. Chirurgicznie usunąć zmienione chorobowo lub uszkodzone płatki zastawki i wszystkie związane z nią struktury konieczne do usunięcia. 2. Chirurgicznie usunąć wapń z pierścienia w celu zapewnienia odpowiedniego umieszczenia pierścienia do wszywania bioprotezy i niedopuszczenia do uszkodzenia delikatnej tkanki płatka. 3. Należy zmierzyć pierścień włóknisty, używając kalibratorów aortalnych Carpentier-Edwards model 1133 (Rysunki 1a-1c).

Krok	Postępowanie
	Przestroga: Podczas doboru wymiarów bioprotezy dla danego pacjenta należy wziąć pod uwagę jego wymiary anatomiczne, wiek i kondycję fizyczną, aby zmniejszyć do minimum możliwość uzyskania suboptymalnego wyniku hemodynamicznego. Jednak ostatecznego doboru bioprotezy w poszczególnych przypadkach powinien dokonać lekarz po starannym rozważeniu wszystkich zagrożeń i korzyści dla określonego pacjenta. **Przestroga: Nie należy stosować kalibratorów protez innych producentów lub kalibratorów przeznaczonych do innych bioprotez Edwards Lifesciences w celu określenia rozmiaru osierdziowej bioprotezy aortalnej Edwards model 11000A.** **Przestroga: Sprawdzić kalibratory pod kątem zużycia, takiego jak stępienie, popękanie lub spękanie włoskowate. Wymienić kalibrator, jeśli widoczne są oznaki zniszczenia.** **Ostrzeżenie: Fragmenty rękojeści i kalibratorów nie są radiologicznie nieprzezroczyste i nie można ich lokalizować za pomocą zewnętrznego urządzenia obrazującego.**
2	Należy zastosować technikę szycia pozwalającą na nadpierścieniowe umieszczenie bioprotezy, taką jak przerywany poziomy ścieg materacowy. Podczas zakładania szwów przez pierścień do przyszywania osierdziowej bioprotezy aortalnej Edwards model 11000A zaleca się, by szwy przechodziły przez pierścień do przyszywania jak najbliżej ramy bioprotezy. Kiedy szwy zostaną założone, należy je przyciąć blisko węzłów, by zapobiec kontaktowi końcówek szwu z tkanką płatka bioprotezy. HVT35 

Krok	Postępowanie
3	Uchwyt z dołączoną do niego rękojeścią zostają usunięte jako całość po zakończeniu procedury zakładania szwów. 1. Za pomocą skalpela należy obciąć każdy z trzech wyeksponowanych szwów znajdujących się na górze uchwytu. HVT36  **Przestroga: Należy uniknąć przecięcia lub uszkodzenia stentu lub delikatnej tkanki płatków podczas przecinania szwów.** 2. Po odcięciu wszystkich trzech szwów przy uchwycie należy usunąć z bioprotezy zespół rękojeść/uchwyt, w całości, wraz ze szwami przy uchwycie. 3. Należy wyjąć rękojeść z uchwytu i wyrzucić uchwyt.

10.5 Czyszczenie i sterylizacja

Akcesoria do osierdziowej bioprotezy aortalnej Edwards, model 11000A są pakowane oddzielnie. Rękojeść model 1126 dostarczana jest jałowa i przeznaczona wyłącznie do jednorazowego użytku. Rękojeść model 1111 oraz kalibratory model 1133 dostarczane są jako niejałowe i muszą być wysterylizowane przed użyciem. Należy wyczyścić i ponownie wysterylizować rękojeści, kalibratory, podstawę i pokrywę tacy przed każdym użyciem. Instrukcje dotyczące mycia i wyjaławiania zawiera instrukcja stosowania dostarczana z akcesoriami wielorazowymi.

10.6 Zwrot bioprotez

Firma Edwards Lifesciences jest zainteresowania otrzymaniem odzyskanych klinicznych egzemplarzy osierdziowej bioprotezy aortalnej model 11000A do analizy. W celu zwrotu odzyskanych bioprotez należy skontaktować się z lokalnym przedstawicielem firmy.

- Nieotwarte opakowanie z nienaruszoną barierą jałową: Jeśli torebka foliowa ani tace nie zostały otwarte, bioprotezę należy zwrócić w oryginalnym opakowaniu.
- Otwarte opakowanie, lecz bioproteza nie została wszczepiona: Jeśli taca została otwarta, bioproteza nie jest już jałowa. Jeśli bioproteza nie zostanie wszczepiona, należy ją umieścić w odpowiednim utrwalaczu histologicznym takim jak 10% formalina lub 2% aldehyd glutarowy i zwrócić do firmy. W takich okolicznościach schłodzenie nie jest konieczne.
- Eksplantowana bioproteza: Eksplantowane bioprotezy należy umieścić w odpowiednim utrwalaczu histologicznym, takim jak 10% formalina lub 2% glutaraldehyd, i zwrócić do firmy. W takich okolicznościach schłodzenie nie jest konieczne.

11. Zasady bezpieczeństwa w środowisku rezonansu magnetycznego (MR)

Warunki w badaniu MR

Badania pozakliniczne wykazały, że osierdziowa bioproteza aortalna Edwards model 11000A może być warunkowo stosowana w środowisku MR. Badanie pacjenta bezpośrednio po wszczepieniu zastawki model 11000A można wykonać bezpiecznie po umieszczeniu tego implantu w następujących warunkach:

- Statyczne pole magnetyczne o indukcji równej 1,5 tesli (T) lub 3 tesli.
- Maksymalny gradient przestrzenny pola magnetycznego 2670 gausów/cm.
- Maksymalny średni specyficzny współczynnik wchłaniania zgłoszony dla systemu rezonansu magnetycznego dla całego ciała (SAR) na poziomie 2,0 W/kg w normalnym trybie działania przez 15 minut skanowania jednej sekwencji.

W badaniach pozaklinicznych, osierdziowa bioproteza aortalna Edwards, model 11000A, dawała szacowany maksymalny wzrost temperatury *in vivo* mniejszy niż lub równy 1,8°C dla maksymalnego zgłoszonego systemu rezonansu magnetycznego, średni specyficzny współczynnik wchłaniania dla całego ciała (SAR) na poziomie 2,0 W/kg, przez 15 minut skanowania MR w systemie rezonansu magnetycznego cewki RF GE Signa 64 MHz (1,5 T) oraz GE Signa HDx (3 T) z wersją oprogramowania 15\LX\MR Software wersja 15.0.M4.0910.a.

Artefakty obrazu mierzono pozaklinicznie w systemie rezonansu magnetycznego GE Signa 3T HDx MR według ASTM F2119-07, stosując określone dla tego systemu sekwencje echa spinowego i gradientu. Obrazy echa spinowego wykazywały jasne i ciemne artefakty, które rozciągały się tak daleko, jak 40 mm od implantu, oraz częściowo lub całkowicie przesłaniały światło. Obrazy gradientu echa wykazywały nieprzezroczyste ciemne lub jasne i ciemne artefakty o trójkątnym kształcie, które rozciągały się tak daleko, jak 40 mm od implantu i całkowicie przesłaniały światło. Możliwa jest redukcja ilości artefaktów przy użyciu sekwencji przeznaczonych do redukcji artefaktów metalu.

12. Informacje dla pacjentów

12.1 Karta identyfikacyjna badania

Karta identyfikacyjna badania jest przekazywana każdemu pacjentowi ze wszczepioną osierdziową protezą aortalną Edwards model 11000A.

12.2 Materiały informacyjne dla pacjenta

Materiały informacyjne dla pacjenta można uzyskać w firmie Edwards lub u przedstawiciela klinicznego firmy Edwards.

13. Piśmiennictwo

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Niniejszy produkt jest wytwarzany i sprzedawany zgodnie z co najmniej jednym spośród następujących patentów amerykańskich: patenty amerykańskie nr: 5,928,281; 5,931,969; 5,961,549; 6,102,944; 6,245,105; 6,413,275; 6,561,970; 6,585,766; 6,837,902; 6,945,997; 7,214,344; 7,972,376; 8,007,992; 8,357,387; 8,366,769; 8,632,608; i RE 40570; oraz odpowiadające patenty zagraniczne. Ponadto trwa uzyskiwanie innych patentów.

Należy zapoznać się z objaśnieniami symboli, umieszczonymi na końcu niniejszego dokumentu.

Tabela 2. Zestawienie współczynników powikłań, model 2700

	Grupa po izolowanej AVR			Populacja DVR		
Powikłanie	**pooperacyjny % pacjentów**	**Okres pooperacyjny % na pacjentorok**	**% wolności od zdarzeń po sześciu latach (błąd standardowy)**	**pooperacyjny % pacjentów**	**Okres pooperacyjny % na pacjentorok**	**% wolności od zdarzeń po sześciu latach (błąd standardowy)**
Zgon	4,7	4,6	73,5 (2,0)	12,9	4,2	67,2 (6,5)
Eksplantacja	0	0,3	98,5 (1,0)	0	0,8	N/D *
Powtórny zabieg operacyjny związany z zastawką	0,7	0,1	99,8 (0,4)	0	0	N/D *
Wszystkie przypadki powtórnej operacji	22,4	1,8	75,4 (1,8)	34,3	2,3	N/D *
Zaburzenia zakrzepowo-zatorowe związane z zastawką	3,1	1,5	91,4 (1,1)	1,4	5,1	N/D *
Wszystkie zdarzenia zakrzepowo-zatorowe	5,0	2,4	84,9 (1,6)	5,7	6,6	N/D *
Zapalenie wsierdzia	0,6	0,8	95,8 (0,9)	1,4	1,5	N/D *
Dysfunkcja zastawki	0,1	0,7	96,0 (1,1)	0	0,4	N/D *
Przeciek okołoza-stawkowy	0,1	0,3	98,8 (0,5)	0	1,2	N/D *
Powikłania krwotoczne leczenia	1,4	0,4	96,4 (1,1)	4,3	2,3	N/D *
Hemoliza	0	0,2	99,1 (0,4)	0	0,4	N/D *
Zakrzepica zastawki	0	0	100,0 (0)	0	0,4	N/D *

* N/D = Nie dotyczy

Tabela 3. Wyniki echokardiografii w okresie pooperacyjnym, model 2700

	Rozmiar zastawki						
	19 mm	**21 mm**	**23 mm**	**25 mm**	**27 mm**	**29 mm**	**Całkowita**
Ogółem N	12	22	15	8	3	3	63
Śr. liczba miesięcy po operacji	28,6 ± 7,2	34,9 ± 8,6	36,9 ± 9,2	39,9 ± 7,6	31,4 ± 15,9	15,3 ± 12,2	34,6 ± 9,2
Prędkość przepływu (m/sek.)							
średnia ± S.D.	2,80 ± 0,49	2,56 ± 0,46	2,36 ± 0,42	2,15 ± 0,56	2,09 ± 0,27	2,08 ± 0,1	2,46 ± 0,50
n =	12	21	15	7	3	3	61
zakres	1,90 - 3,60	1,90 - 3,90	1,39 - 2,86	1,00 - 2,60	1,90 - 2,40	2,05 - 2,10	1,00 - 3,90
Chwilowa wartość szczytowa gradientu (mmHg)							
średnia ± S.D.	32,22 ± 11,08	27,04 ± 10,49	23,00 ± 7,30	19,50 ± 8,16	17,60 ± 4,70	14,4 ± 0,58	25,67 ± 10,14
n =	12	21	15	7	3	3	61
zakres	14,40 - 51,80	14,40 - 60,80	7,70 - 32,70	4,00 - 27,00	14,40 - 23,00	13,95 - 15,06	4,00 - 60,80

Tabela 4. Wyniki skuteczności, klasa czynnościowa NYHA, model 2700

Okres przedoperacyjny Klasa czynnościowa NYHA	Okres pooperacyjny Klasa czynnościowa NYHA					
	I	II	III	IV	Zgon	Brak dostępnych danych
I	18	19			9	
II	140	37			35	15
III	181	48	4	1	72	24
IV	43	16	2		53	2
Niedostępne	5	1			2	2

Tabela 5. Współczynniki wolności od powikłań po 20 latach (n = 267), model 2700

Wolność od powikłań po 20 latach	Faktyczna	Aktuarialna	Liniowa (%/pacjentorok)
Zgony związane z zastawką	85,8 ± 2,5%	67,9 ± 6,6%	1,2
Zaburzenia zakrzepowo-zatorowe/zakrzepica	82,4 ± 2,6%	68,2 ± 6,8%	1,7
Krwawienie	94,0 ± 1,5%	91,7 ± 2,2%	0,4
Zapalenie wsierdzia/posocznica	91,7 ± 1,7%	89,3 ± 2,4%	0,8
Eksplantacja spowodowana SVD			
≥ 60	92,6 ± 2,0%	77,1 ± 7,2%	b/z*
≥ 65	96,3 ± 1,6%	81,5 ± 9,6%	
> 70	96,0 ± 2,3%	69,9 ± 20,5%	

** Bez znaczenia. SVD nie występuje jako stała funkcja ryzyka; w rezultacie liniowe współczynniki nie są istotne.*

Tabela 6. Podsumowanie zdarzeń niepożądanych związanych z zastawką, modele 3000 oraz 3000TFX

	≤ 30 dni po operacji		> 30 dni po operacji	
Zdarzenia niepożądane	**3000TFX (N = 193) liczba zdarzeń (% pacjentów)**	**3000/3000TFX (N = 253) liczba zdarzeń (% pacjentów)**	**3000TFX (N = 193) liczba zdarzeń (% pacjentów)**	**3000/3000TFX (N = 253) liczba zdarzeń (% pacjentów)**
Zaburzenia zakrzepowo-zatorowe związane z zastawką	6 (3,1)	7 (2,8)	3 (2,0)	3 (1,4)
Niestrukturalna dysfunkcja zastawki (PVL)	3 (1,5)	4 (1,6)	3 (2,0)	3 (1,4)
Eksplantacja (NSVD)	2 (1,0)	2 (0,8)	0 (0,0)	0 (0,0)
Zgon (zatrzymanie akcji serca, zdarzenie typu krwawienie, CVA)	1 (0,5)	1 (0,4)	3 (2,0)	3 (1,4)
Powtórny zabieg operacyjny	1 (0,5)	1 (0,4)	1 (0,7)	1 (0,5)
Hemoliza	1 (0,5)	1 (0,4)	3 (2,0)	3 (1,4)
Krwawienie związane z AC	0 (0,0)	0 (0,0)	2 (1,4)	2 (1,0)
Zapalenie wsierdzia	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Strukturalne pogorszenie stanu zastawki	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Zakrzepica zastawki	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Inne (rozdarcie aorty)	1 (0,5)	1 (0,4)	0 (0,0)	0 (0,0)

Tabela 7. Zmienne hemodynamiczne w elektrokardiogramach dla kontroli po 1 roku, modele 3000 i 3000TFX

Rodzaj zastawki	Parametr	19 mm Średnia ± SD (n)	21 mm Średnia ± SD (n)	23 mm Średnia ± SD (n)	25 mm Średnia ± SD (n)	27 mm Średnia ± SD (n)	29 mm Średnia ± SD (n)
3000TFX	Średni gradient ciśnienia skurczowego (mmHg)	16,7 ± 4,7 (10)	15,8 ± 4,4 (18)	11,3 ± 3,7 (45)	11,1 ± 4,1 (37)	9,4 ± 4,3 (12)	9,0 ± 0,0 (2)
	Frakcja wyrzutowa (%)	65,8 ± 10,4 (10)	62,7 ± 9,4 (19)	60,6 ± 11,3 (48)	61,4 ± 11,2 (38)	59,5 ± 10,7 (12)	55,0 ±14,1 (2)
	EOA aorty (cm^2)	1,2 ± 0,4 (10)	1,5 ± 0,4 (18)	1,8 ± 0,6 (44)	1,8 ± 0,5 (36)	2,1 ± 0,6 (12)	2,1 ± 0,1 (2)
3000/ 3000TFX	Średni gradient ciśnienia skurczowego (mmHg)	16,7 ± 4,2 (16)	13,8 ± 4,8 (34)	11,7 ± 4,7 (56)	11,0 ± 3,8 (47)	9,5 ± 4,1 (14)	9,0 ± 0,0 (2)
	Frakcja wyrzutowa (%)	62,1 ± 15,1 (16)	58,6 ± 11,6 (34)	60,2 ± 11,2 (59)	60,2 ± 11,5 (47)	58,5 ± 10,5 (14)	55,0 ± 14,1 (2)
	EOA aorty (cm^2)	1,3 ± 0,5 (16)	1,5 ± 0,4 (32)	1,8 ± 0,6 (55)	1,8 ± 0,6 (46)	2,1 ± 0,6 (14)	2,1 ± 0,1 (2)

Tabela 8. Klasa czynnościowa NYHA: Zmiana względem wartości wyjściowych dla wizyty kontrolnej po 1 roku, modele 3000 i 3000TFX

		-----Wartości wyjściowe-----				
Rodzaj zastawki	**Klasa NYHA w okresie obserwacji**	**Klasa I**	**Klasa II**	**Klasa III**	**Klasa IV**	**Nie dotyczy**
3000TFX N = 193	**Klasa I**	10	33	51	10	3
	Klasa II	2	8	13	2	1
	Klasa III	-	-	3	-	-
	Klasa IV	-	-	-	1	-
	Zgon	-	3	16	1	-
	Eksplantacja	-	-	3	-	-
	Nie dotyczy	2	6	21	4	-
3000/ 3000TFX N = 253	**Klasa I**	12	40	71	11	3
	Klasa II	2	14	29	3	1
	Klasa III	-	-	3	-	-
	Klasa IV	-	-	1	1	-
	Zgon	-	3	19	2	-
	Eksplantacja	-	-	3	-	-
	Nie dotyczy	2	7	22	4	-

Klasa czynnościowa NYHA: Zmiana względem wartości wyjściowych dla wizyty kontrolnej po 1 roku

Rodzaj zastawki	Poprawa N (%)	Bez zmian N (%)	Pogorszenie N (%)	Nie dotyczy N (%)
3000TFX (N = 193)	109 (56,5)	22 (11,4)	2 (1,0)	60 (31,1)
3000/3000TFX (N = 253)	154 (60,9)	30 (11,9)	3 (1,2)	66 (26,1)

Symbol Legend • Légende des symboles • Legenda Symboli

	English	Français	Polski
REF	Catalogue Number	Numéro de référence	Numer Katalogowy
⚠	Caution	Attention	Przestroga
	Consult instructions for use	Consulter le mode d'emploi	Zapoznać się z instrukcją użycia
2	Single Use	À usage unique	Do jednorazowego użytku
#	Quantity	Quantité	Ilość
	Use By	Utiliser avant	Zużyć Do
SN	Serial Number	Numéro de série	Numer Serii
	Manufacturer	Fabricant	Producent
SZ	Size	Taille	Rozmiar

	English	Français	Polski
STERILE EO	Ethylene Oxide Sterilized	Stérilisé à l'oxyde d'éthylène	Wysterylizowano Przy Użyciu Tlenku Etylenu
	Do not use if package is opened or damaged.	Ne pas utiliser si l'emballage est ouvert ou endommagé.	Nie używać, jeśli opakowanie jest otwarte lub uszkodzone.
EC REP	European Authorized Representative	Mandataire européen	Autoryzowany przedstawiciel w Europie
STERILE	Contents sterile and nonpyrogenic if package is unopened or undamaged.	Contenu stérile et apyrogène si le conditionnement n'est ni ouvert ni endommagé.	Zawartość sterylna i niepirogenna, o ile opakowanie nie zostało otwarte ani uszkodzone.
25 °C 10 °C	Do not freeze - Store between 10 °C and 25 °C	Ne pas congeler - Conserver entre 10 °C et 25 °C	Nie zamrażać - Przechowywać w temperaturze od 10 °C do 25 °C

Note: Not all symbols may be included in the labeling of this product. • **Remarque :** il est possible que certains symboles n'apparaissent pas sur les étiquettes de ce produit. • **Uwaga:** Nie wszystkie symbole muszą być użyte na etykietach niniejszego produktu.

GLX3SL5x7.1

EC REP

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Edwards Irvine, CA 92614	Title: IFU, 11000A, IDE, E, F, P		
	Part Number: 156983003 Rev.: A	Page 41 of 41	ECR: 118875
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NOTE
1. ALL ART PRINTS 100% BLACK UNLESS OTHERWISE NOTED.

INK
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Edwards Lifesciences

DIRECTORY

English

Edwards Pericardial Mitral Bioprosthesis, Model 11000M

Instructions for use

CAUTION: Investigational Device. Limited by Federal (United States) law to Investigational Use.

CAUTION: Investigational device. Exclusively for Clinical Investigations.

Caution: Investigational Device. Limited to Investigational Use. To be used by Qualified Investigators (Physicians).

1. Device and Accessories Description

1.1 Device Description

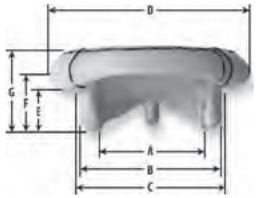
The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is a trileaflet bioprosthesis comprised of treated bovine pericardium that is mounted on a flexible frame. It is available in sizes 25, 27, 29, 31, and 33 mm (Table 1). The bioprosthesis is stored in non-aqueous packaging, and does not require rinsing prior to implantation.

The wireform is made of a cobalt chromium alloy covered with a woven polyester fabric. A cobalt-chromium alloy/polyester film laminate band surrounds the base of the wireform frame.

A waffled silicone sewing ring that is covered with a porous polytetrafluoroethylene (PTFE) cloth is attached to the wireform frame. The sewing ring is scalloped along its anterior portion. Black silk suture markers on the anterior portion facilitate the orientation of the bioprosthesis and help avoid obstruction of the left ventricular outflow tract by a strut.

A black silk suture guide line circles the sewing ring. Placing sutures through the sewing ring and in the region from the suture guide line to the outer portion of the sewing ring eases needle penetration and provides variable compliance. The waffle has wider cells along the posterior portion, where calcifications or irregularities of the native mitral annulus are more frequent (Ref. 6).

Table 1. Nominal Dimensions



HVT63

Size	25 mm	27 mm	29 mm	31 mm	33 mm
A. Stent Diameter (Wireform, mm)	25	27	29	31	31
B. Tissue Annulus Diameter (mm)	28	29.5	31.5	33.5	33.5
C. External Stent Post Diameter (Tip, mm)	29	31	34	35	35
D. External Sewing Ring Diameter (mm)	36	38	40	42	44
E. Effective Profile Anterior (mm)	7	7.5	8	8.5	8.5
F. Effective Profile Posterior (mm)	10	10.5	11	11.5	11.5
G. Total Profile Height (mm)	15	16	17	18	18
Geometric Orifice Area (mm^2)	424	499	580	653	653

1.2 Accessories Description

Accessories available for use with the 11000M bioprosthesis are:

- Tricentrix holder system
- Replica Sizer 1173R
- Barrel Sizer 1173B
- Sterilization Tray provided in model SET1173
- Handle models 1111, 1117, 1173, and 1126 (single use)

All accessories are supplied non-sterile, except for the Tricentrix holder system that is supplied sterile attached to the sterile bioprosthesis, and the handle 1126 that is supplied sterile and is for single use only.

Sizers and Tray

Only sizers model 1173B (Figure 1a) or 1173R (Figure 1b) may be used with the 11000M bioprosthesis.

Caution: Do not use other manufacturer's valve sizers, or sizers for other Edwards Lifesciences valve prostheses to size the 11000M bioprosthesis.

Use only the sizers model 1173B or 1173R to determine the appropriate 11000M bioprosthesis size. Sizers model 1173B and 1173R permit direct observation of their fit within the annulus and are provided for each available 11000M bioprosthesis size. The barrel of the sizers model 1173B and 1173R indicate the

external stent diameter at the base. The lip of the replica sizer 1173R replicates the sewing ring of the bioprosthesis, with its scalloped anterior portion and black markings, to determine the outcomes of specific suture or subvalvular apparatus preservation techniques.

The sizers 1173B and 1173R are labeled with the bioprosthesis size. The complete set of sizers is housed in a tray, model SET1173, which can be reused and resterilized.

Figure 1a – 1173B Barrel Sizer

CP1089-16

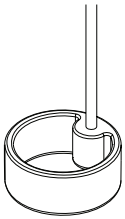
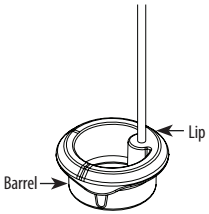


Figure 1b – 1173R Replica Sizer

CP1089-15

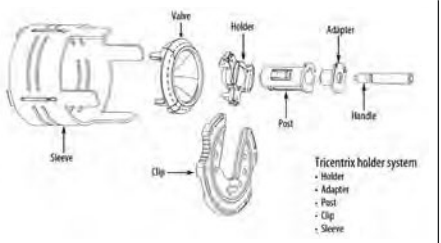


Tricentrix Holder System and Handles

The holder/handle assembly consists of two components: the Tricentrix holder system (Figure 2) that is mounted to the 11000M bioprosthesis, and a handle (1111, 1117, 1173, or 1126) that is attached to the Tricentrix holder system at the time of surgery.

Figure 2 – Tricentrix Holder System

CP1089-28



HVT55

The following handles (Table 2) may be used with the 11000M Bioprosthesis:

Table 2. Accessory Handles

Model	Shaft Material	Overall Length inch	Overall Length cm	Reusable
1111	Stainless steel	7.0	17.8	Yes
1117	Nitinol	9.1	23.2	Yes
1126	Stainless steel	11.5	29.2	No
1173	Nitinol	11.3	28.6	Yes

Handles with a nitinol shaft are more flexible than stainless steel. With each sterilization cycle, they return to their original straight shape for easier attachment to the holder.

2. Indications for Use

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M is indicated for patients who require replacement of their native or prosthetic mitral valve.

3. Contraindications

Do not use if the surgeon believes such would be contrary to the best interests of the patient. The actual decision for or against the use of this bioprosthesis must remain with the surgeon who can evaluate all the various risks involved, including the anatomy and pathology observed at the time of surgery.

4. Warnings

FOR SINGLE USE ONLY. This device is designed, intended, and distributed for single use only. Do not re-sterilize or reuse this device. There are no data to support the sterility, nonpyrogenicity, and functionality of the device after sterile reprocessing. Exposure of the bioprosthesis or package to irradiation, steam, ethylene oxide, or other chemical sterilants will render the bioprosthesis unfit for use.

DO NOT FREEZE OR EXPOSE THE BIOPROSTHESIS TO EXTREME HEAT. Exposure of the bioprosthesis to extreme temperatures will render the device unfit for use.

DO NOT USE the bioprosthesis:

- **If the foil pouch, sealed trays, or lids are opened, damaged, or stained**
- **If the expiration date has elapsed, or**
- **If it has been dropped, damaged, or mishandled in any way. Should a bioprosthesis be damaged during insertion, do not attempt repair.**

DO NOT EXPOSE the bioprosthesis to any solutions, chemicals, antibiotics, etc., except for sterile physiological saline solution. Irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.

DO NOT GRASP the leaflet tissue of the bioprosthesis with instruments or cause any damage to the bioprosthesis. Even the most minor leaflet tissue perforation may enlarge in time to produce significant impairment of valve function.

DO NOT OVERSIZE. Oversizing may cause bioprosthesis damage or localized mechanical stresses, which may in turn injure the heart or result in leaflet tissue failure, stent distortion and valve regurgitation.

DO NOT PASS CATHETERS, transvenous pacing leads, or any surgical instrument across the bioprosthesis with the exception of a surgical mirror used to examine struts and suture placement. Other surgical devices may cause leaflet tissue damage.

As with any implanted medical device, there is a potential for patient immunological response. Some components of the model 11000M are a metal alloy that contains cobalt, chromium, nickel, molybdenum, manganese, carbon, beryllium and iron. Care should be exercised in patients with hypersensitivities to these materials. This device was manufactured without latex, but may have been produced in a latex-containing environment.

5. Adverse Events

5.1 Observed Adverse Events

As with all prosthetic heart valves, serious adverse events, sometimes leading to death, may be associated with the use of tissue valves. In addition, adverse events due to individual patient reaction to an implanted device or to physical or chemical changes to the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device.

The Edwards Pericardial Mitral Bioprosthesis Model 11000M is similar in design to the Carpentier-Edwards PERIMOUNT Magna Mitral Ease pericardial bioprostheses model 7300TFX.

Three (3) multi-center, non-randomized, prospective non-US clinical studies were conducted with the mitral pericardial bioprosthesis model 6900. Three hundred one (301) patients had isolated mitral valve replacement (MVR) and 62 patients had double valve replacement (DVR), where the aortic valve was replaced with a Carpentier-Edwards PERIMOUNT pericardial bioprosthesis aortic model.

In the first study, bioprostheses were implanted between 1984 and 1986; in the second study, bioprostheses were implanted between 1989 and 1994; and in the third study, bioprostheses were implanted between 1996 and 1997. Patients were evaluated preoperatively, intraoperatively, at discharge, at 1 year, and annually thereafter. Adverse events were captured throughout the postoperative period.

Table 3 presents the observed rates for early events (≤ 30 days for valve-related adverse events), the linearized rates for late events (> 30 days postoperatively), and the actuarial adverse event rates at 1, 5, and 8 years postoperatively for model 6900. The adverse event rates were based on 363 patients at nine centers. The cumulative follow-up was 1100 patient-years with a mean follow-up of 3.0 years (SD = 2.4 years, range = 0 to 8.2 years). Preoperative and operative patient demographics are presented in Tables 5 and 7. Effectiveness results are presented in Tables 9 and 11.

One (1) multi-center, non-randomized, prospective international clinical study was conducted with patients implanted with the Carpentier-Edwards PERIMOUNT Plus pericardial bioprosthesis model 6900P mitral. One hundred seventy five (175) patients had isolated mitral replacement (MVR) and 34 patients had double valve replacement (DVR), where the aortic valve was replaced with a Carpentier-Edwards PERIMOUNT pericardial bioprosthesis aortic model. In this study, patients were implanted between 1999 and 2007. Patients were evaluated preoperatively, intraoperatively at discharge, at 1 year, and annually thereafter. Adverse events were captured throughout the postoperative period. Table 4 presents the observed rates for early events (≤ 30 days for valve related adverse events), the linearized rates for late events (> 30 days postoperatively), and the actuarial adverse event rates at 1- and 5-years postoperatively for model 6900P. The adverse event rates were based on two hundred nine (209) patients at seven centers. The cumulative follow-up was 873.18 patient-years with a mean follow-up of 4.2 years (SD = 2.3 years, range = 0 to 8.2 years). Preoperative and operative patient demographics are presented in Tables 6 and 8. Effectiveness results are presented in Tables 10 and 12.

5.2 Potential Adverse Events

Adverse events potentially associated with the use of bioprosthetic heart valves include:

- Angina
- Bleeding diatheses (coagulopathy) related to anticoagulant therapy
- Cardiac arrhythmias
- Coronary ostial blockage
- Endocarditis
- Heart failure
- Hemolysis
- Hemolytic anemia
- Hemorrhage
- Local and/or systemic infection
- Myocardial infarction
- Patient prosthetic mismatch (PPM)
- Prosthesis leaflet entrapment (Impingement)
- Prosthesis nonstructural dysfunction
- Prosthesis pannus
- Prosthesis perivalvular leak
- Prosthesis regurgitation
- Prosthesis structural deterioration
- Prosthesis thrombosis
- Stroke
- Thromboembolism
- Transient ischemic attack (TIA)

It is possible that these complications could lead to:

- Reoperation
- Explantation
- Permanent disability
- Death

Other adverse events associated with the use of Carpentier-Edwards PERIMOUNT mitral pericardial bioprostheses model 6900 compiled from the literature and from reports received through the Edwards Lifesciences complaint handling system include: stenosis, regurgitation through an incompetent valve, ventricular perforation by stent posts, malfunctions of the valve due to distortion at implant, and fracture of the wireform frame.

6. Clinical Studies

The safety endpoints captured in the prospective studies were adverse events; blood analyses were used to confirm the absence or presence of certain adverse events. The safety results for model 6900 are provided in Table 3 and for model 6900P in Table 4. Preoperative patient demographics for model 6900 are provided in Table 5 and for model 6900P in Table 6. Operative patient demographics for model 6900 are provided in Table 7 and for model 6900P in Table 8. Effectiveness endpoints were New York Heart Association (NYHA) functional classification summarized in Table 9 for model 6900 and Table 10 for

model 6900P and echocardiographic assessments summarized in Table 11 for model 6900 and Table 12 for model 6900P.

There are no clinical data presently available demonstrating increased resistance of the Edwards Pericardial Mitral Bioprosthesis Model 11000M to calcification as compared to other commercially available bioprostheses.

7. Individualization of Treatment

Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial stages after implantation, as determined by the physician on an individual basis. Long-term anticoagulant and/or antiplatelet therapy should be considered for patients with risk factors for thromboembolism.

The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all the circumstances presented by that patient (Ref. 7). A bioprosthesis is recommended for MVR in patients of any age who will not take warfarin or who have major medical contraindications to warfarin therapy. Patient preference is a reasonable consideration in the selection of mitral valve operation and valve prosthesis. A mechanical prosthesis is reasonable for MVR in patients under 65 years of age who do not have a contraindication to anticoagulation. A bioprosthesis is reasonable for MVR in patients under 65 years of age who elect to receive this valve for lifestyle considerations after detailed discussions of the risks of anticoagulation versus the likelihood that a second MVR may be necessary (Ref. 7).

7.1 Specific Patient Populations

The safety and effectiveness of the Model 11000M bioprosthesis has not been established for the following specific populations because it has not been studied in these populations:

- patients who are pregnant;
- nursing mothers;
- patients with abnormal calcium metabolism (e.g., chronic renal failure, hyperparathyroidism);
- patients with aneurysmal aortic degenerative conditions (e.g., cystic medial necrosis, Marfan's syndrome);
- children, adolescents, and young adults

Caution: Based on reports in the literature on tissue valves (Refs. 9, 10, 11, 12 & 13), there appears to be an increased incidence of leaflet calcification in patients under the age of 20. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period, and excessive milk or dairy product consumption should be avoided in children. Animal research studies (Ref. 14) show that a high systemic calcium level can lead to early calcification.

8. Patient Counseling Information

Careful and continued medical follow-up (at least by an annual visit to the physician) is advised so that bioprosthesis-related complications, particularly those related to material failure, can be diagnosed and properly managed. Patients with bioprostheses are at risk from bacteremia (e.g., undergoing dental procedures) and should be advised about prophylactic antibiotic therapy. Patients should be encouraged to carry their Patient Identification Card at all times and to inform their healthcare providers that they have an implant when seeking care.

9. How Supplied

9.1 Packaging

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is provided sterile and non-pyrogenic, in a double barrier tray package. The double tray package is in a foil pouch, which is in a carton.

Each bioprosthesis is contained in a carton with a temperature indicator displayed through a window on the side panel. The temperature indicator is intended to identify products which have been exposed to transient temperature extremes. Upon receipt of the bioprosthesis, immediately inspect the indicator and refer to the carton label to confirm a "Use" condition. If the "Use" condition is not apparent, do not use the bioprosthesis and contact the local supplier or Edwards Lifesciences representative to make arrangements for return authorization and replacement.

Warning: Carefully inspect the bioprosthesis before implantation for evidence of extreme temperature exposure or other damage.

9.2 Storage

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, should be stored at 10 °C to 25 °C (50-77 °F), in the foil pouch and shelf carton.

10. Directions for Use

10.1 Physician Training

The techniques for implanting this bioprosthesis are similar to those for implanting any stented mitral bioprosthesis. No special training is required to implant the Edwards Pericardial Mitral Bioprosthesis, Model 11000M.

10.2 Sizing

Caution: Do not use other manufacturer's valve sizers, or sizers for other Edwards Lifesciences valve prostheses to size the 11000M bioprosthesis.

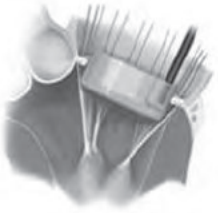
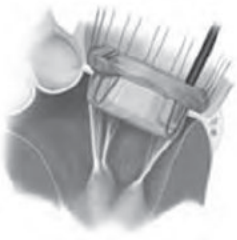
Caution: Examine sizers and handles for signs of wear, such as dullness, cracking or crazing. Replace sizer or handle if any deterioration is observed.

Warning: Fragments of handles and sizers are not radiopaque and cannot be located by means of an external imaging device.

Verify that the accessories have been sterilized according to the recommended instructions provided with the reusable accessories.

The black marks on the lip replicate the black suture markers on the sewing ring. They delimit the anterior portion of the bioprosthesis sewing ring which should be positioned across the anterior intercommissural portion of the native annulus, in order to straddle the left ventricular outflow tract area. The height and location of the stent posts are marked on the replica sizer 1173R to aid in assessing optimal alignment and seating.

The sizers include pre-attached handles with increased handle length for improved access in the case of a difficult exposure, a deep thoracic cage or minimally invasive access. The posterior handle attachment to the sizer allows an unobstructed view through the barrel into the ventricle for assessment of subvalvular structures. The sizers 1173B and 1173R are labeled with the bioprosthesis size.

Step	Procedure
1	**Sizing with barrel sizer 1173B:** To size with barrel sizer 1173B, pass the barrel portion of the sizer through the mitral annulus. Ensure the barrel portion is directly in plane of the mitral annulus. HVT60 
2	**Sizing with replica sizer 1173R:** To size with replica sizer 1173R, pass the barrel portion of the replica sizer through the mitral annulus so that the tip of the sizer, which simulates the sewing ring portion of the bioprosthesis, rests on the superior aspect of the annulus. HVT61 

Some techniques such as use of pledgets, leaflet reefing, or mitral subvalvular apparatus preservation may further reduce the size of the mitral annulus which can result in the need for a smaller bioprosthesis to be implanted (Ref. 8). When using these techniques, it is recommended to re-size the annulus to avoid oversizing of the bioprosthesis. The consistent performance of the Edwards Pericardial Mitral Bioprostheses, Model 11000M makes oversizing unnecessary to achieve the desired hemodynamic performance in most patients (Table 11 and 12).

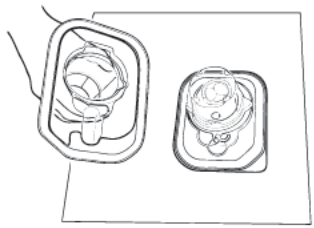
Due to the elastic nature of a chord, it may be extended by the Tricentrix holder system during implantation but retract back around the post once the holder is removed, entrapping leaflets and impairing function. Sizers 1173B and 1173R are made of a transparent material to allow visualization of the subvalvular apparatus during sizing. Make sure no chord will be in the way of the struts.

Caution: Exercise special care when using subvalvular apparatus preservation techniques to avoid chordae entrapment by a strut.

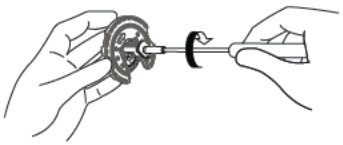
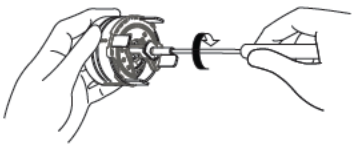
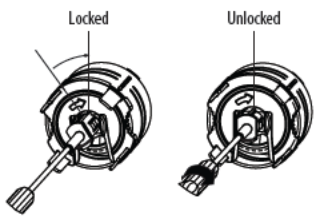
Warning: Avoid oversizing the bioprosthesis. Oversizing may cause bioprosthesis damage or localized mechanical stresses, which may in turn injure the heart or result in leaflet tissue failure, stent distortion and regurgitation.

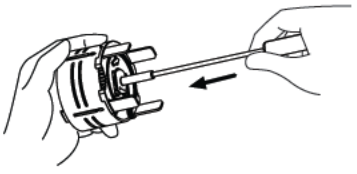
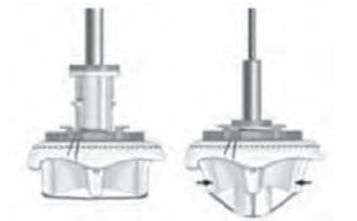
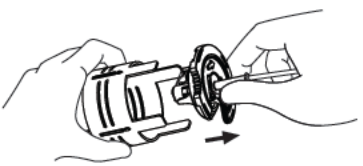
10.3 Handling and Preparation Instructions

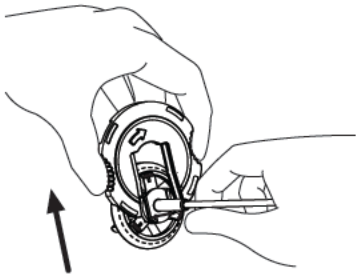
In-service training is recommended prior to handling and preparing the Edwards Pericardial Mitral Bioprosthesis, Model 11000M.

Step	Procedure
1	**Caution: Do not open the Edwards Pericardial Mitral Bioprosthesis, Model 11000M package until implantation is certain.** **Warning: Do not open foil pouch into sterile field. Foil pouch is protective cover only. Only the innermost package tray may be introduced into the sterile field.** Once the appropriate size bioprosthesis is chosen, remove the foil pouch from the carton in the non-sterile field. Before opening, examine the package for evidence of damage and broken or missing seals.
2	Near the sterile field, hold the base of the outer tray and peel the lid from the outer tray.
3	The inner tray and contents are sterile. Transfer the inner tray to the sterile field. The contents of the inner tray must be handled using a sterile surgical technique to prevent contamination. HVT26 
4	**Caution: Do not open the inner package until implantation is certain and the surgeon is ready to place the valve.** **Caution: The bioprosthesis is not secured to the inner tray. Care should be taken while peeling the lid and removing the plastic cover.** Before opening, examine the inner tray and lid for evidence of damage, stains, and broken or missing seals. Hold the base of the inner tray and peel the lid from the inner tray.

Step	Procedure
5	To access the bioprosthesis, remove the plastic cover by pulling up on both tabs. Discard the plastic cover. HVT58  HVT54 
6	Attach the handle to the Tricentrix holder system while the bioprosthesis is still in the tray. To attach, insert the handle into the holder and turn it clockwise until a positive resistance is felt. HVT52  **Caution: Do not grasp the bioprosthesis with hands or surgical instruments.** **Caution: Care should be taken to avoid entangling the serial tag in the handle during attachment.** **Caution: The handle/holder assembly is required for implantation and should not be removed until the bioprosthesis is sutured to the annulus.**

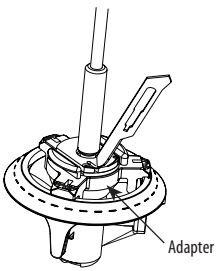
Step	Procedure
7	Once the handle is attached, remove the whole assembly (i.e., plastic sleeve, clip, the Tricentrix holder system and bioprosthesis) from the tray. The plastic sleeve is loosely fitted to the clip and may remain in the tray. This will not affect deployment. HVT53  Grasping the plastic sleeve or clip continue the rotation to overcome the resistance until the white holder post reaches the unlock position. CP1089-23  Or CP1089-6  CP1089-8 CP1089-9 

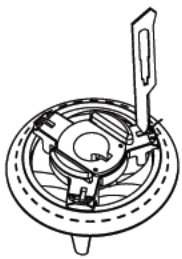
Step	Procedure
8	Apply the required push force on the handle until the white holder post slides across the leaflets and snaps into its fully deployed position. An audible click may be heard as the deployed position is reached. CP1089-24 
9	**Caution: If an adequate push force is not applied to the handle when deploying the Tricentrix holder system, the tenting system will not be secured and will not be able to minimize the potential for suture entrapment.** Always check for proper deployment. There should be no more space between the blue adapter and the grey holder. The handle/post assembly should no longer be able to slide. The white holder post should protrude through the leaflets while the three commissures should deflect slightly towards the center of the bioprosthesis. The leaflets will temporarily be wrinkled by the deployed white holder post. When the holder is removed following implantation, the leaflets will return to their normal position. HVT56 
10	After deployment, remove the sleeve (if attached) by holding the handle and pulling the sleeve off the clip. CP1089-25 

Step	Procedure
11	Remove the clip by sliding it off the holder in a sideways direction. CP1089-26  Both sleeve and clip should be discarded.
12	A serial number tag is attached to the sewing ring of each bioprosthesis by a suture. This serial number should be confirmed with the number on the bioprosthesis package and bioprosthesis implant data card. This tag should not be detached from the bioprosthesis until implantation is certain. **Caution: If any difference in serial number is noted, the bioprosthesis should be returned unused.** **Caution: Care should be exercised to avoid cutting or tearing the sewing ring cloth during removal of the serial number tag.** **Caution: To prevent damage to the sewing ring cloth, avoid pulling the knot of the serial tag suture through the sewing ring.**
13	The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, **DOES NOT REQUIRE RINSING** prior to implantation. **Caution: If the bioprosthesis is rinsed prior to implantation, it must then be kept hydrated with sterile physiological saline irrigation on both sides of the leaflet tissue throughout the remainder of the surgical procedure. Rinsing every one to two minutes is recommended.** **Caution: Avoid contact of the leaflet tissue with towels, linens, or other sources of particulate matter that may be transferred to the leaflet tissue.**

10.4 Device Implantation

Step	Procedure
1	The surgeon should be familiar with the recommendations for proper sizing and placement in the supra-annular position (See 10.2 Sizing). Because of the complexity and variation of cardiac valve replacement surgery, the choice of surgical technique, appropriately modified in accordance with the previously described **Warnings**, is left to the discretion of the individual surgeon. In general, the following steps should be employed: 1. Surgically remove the diseased or damaged valve leaflets and all associated structures deemed necessary. 2. Surgically remove any calcium from the annulus to ensure proper seating of the sewing ring of the bioprosthesis to avoid damage to the delicate leaflet tissue. 3. Proper sizing. Measure the annulus using only the mitral sizer models 1173B and 1173R (Figures 1a-1b). 4. Proper seating of the prosthesis; 5. Tying sutures with the holder in place to minimize the potential for suture looping or chordal entrapment; 6. Examination of the bioprosthetic leaflets for distortion or leak during tying. **Caution: When choosing a bioprosthesis for a given patient, the size, age, and physical condition of the patient in relation to the size of the bioprosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a bioprosthesis, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient.** **Caution: Adequate removal of calcium deposits from the patient's annulus must be performed before implantation to avoid damage to the delicate bioprosthesis leaflet tissue as a result of contact with calcium deposits. Insert the sizer into the mitral annulus. The barrel of the sizer should always fit comfortably in the annulus.** **Caution: Use only sizers 1173B or 1173R during the selection of the bioprosthesis size; other sizers may result in improper valve selection (see 1.2 Accessory Description). Like other mitral bioprostheses, the Edwards Pericardial Mitral Bioprosthesis, Model 11000M is usually implanted using pledgeted mattress sutures. It is recommended to size the annulus after the sutures have been placed, as sutures may decrease the size of the bioprosthesis that can be implanted.**

Step	Procedure
2	**Proper orientation of the bioprosthesis:** **Caution: The wireform frame of the Model 11000M bioprosthesis is symmetrical, and the three commissure supports (struts) are equally spaced. However, the sewing ring is designed for a specific orientation of the bioprosthesis. The scalloped part of the sewing ring, between the two silicone protrusions, should be placed across the intercommissural anterior portion of the annulus and straddle the left ventricular outflow tract.** The contrasting suture markers in the sewing ring are intended to aid in proper orientation and denote a typical intercommissural distance. However, this distance may vary for each individual patient. On the left side, two close black sutures indicate where the first stitch should be placed and correspond to the anterior commissure. On the right side, only one black suture indicates the approximate location of the posterior commissure. Using these orientation aids, the third post should naturally fall in place in or around the middle of the posterior leaflet location. **Caution: Special care must be exercised to avoid placing a strut in front of the left ventricular outflow tract, as it may impair the long-term hemodynamic performance.**
3	**Suture Placement:** A black suture guide line circles the sewing ring. When placing sutures through the sewing ring, sliding drag forces are reduced when sutures are placed straight through the sewing ring and in the region from the suture guide line to the outer portion of the sewing ring. Firm tension must be maintained on the sutures as the bioprosthesis is lowered into the annulus; this minimizes the potential for formation of suture loops that might entrap a leaflet. This, when combined with the fully retracted stent posts when the Tricentrix holder system is in place, helps guide the sutures into their correct position behind the struts and onto the sewing ring. Remove the handle prior to tying the sutures. The handle and blue adapter must be removed as an assembly. Maintain the bioprosthesis placement in the annulus by gently placing forceps or gloved hands onto the holder and cutting the green thread on the blue adapter. Remove the blue adapter and handle assembly as one unit. CP1089-27 

Step	Procedure
4	**Caution: Avoid looping or catching a suture around the open cages, free struts, or commissure supports of the bioprosthesis, which would interfere with proper valvular function. To minimize the potential for suture looping, it is essential to leave the deployed holder in place until all knots are tied.** However, if leaving the holder in place obstructs the surgeon's view, all the sutures adjacent to each of the three frame struts must be tied down before cutting the three green holder attachment threads to remove the holder. **Caution: If the deployed holder attachment threads are cut before these adjacent sutures are tied down, the holder will no longer minimize the potential for suture looping around the frame struts.** Special attention must be given to avoid tying the sutures on top of the corners of the holder's grey legs. Before tying each suture, examine the leaflets while holding the two strands of the suture under tension. Distortion or movement of the leaflets during this maneuver suggests that the suture is looped around a strut. At no point before or after holder removal should tension on the sutures be released as this may facilitate formation of loops in the sutures and possible entrapment. It is recommended to place a surgical mirror through the leaflets after the holder removal in order to examine each strut and proper suture placement. **Caution: When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue (Ref. 8).** The Tricentrix holder system is removed as a unit at the completion of the suturing procedure as follows: CP1089-14  1. Cut each of the three (3) exposed green sutures using a scalpel or scissor placed only in the cutting channel. Never attempt to cut a suture below a partially separated holder as a part of the attaching suture may fall in the ventricle. Avoid cutting or damaging the stent or leaflet tissue when cutting the sutures. 2. When all three (3) attaching sutures have been properly cut, remove the Tricentrix holder system from the bioprosthesis as a unit, along with attaching sutures, using sterile gloved hands or protected forceps. 3. Following implant, remove the holder and discard.

10.5 Accessory Cleaning and Sterilization

The accessories for the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, are packaged separately. Handle model 1126 is provided sterile and is intended for single use only. Handle models 1111, 1117 and 1173 and sizer models 1173B and 1173R are supplied nonsterile and must be cleaned and sterilized before use. The handles, sizers, tray base and tray lid must be cleaned and resterilized prior to each use. Refer to the Instructions for Use supplied with the reusable accessories for cleaning and sterilization instructions.

10.6 Return of Bioprostheses

Edwards Lifesciences is interested in obtaining recovered clinical specimens of the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, for analysis. Contact the local representative for return of recovered bioprostheses.

- Unopened Package with Sterile Barrier Intact: If the foil pouch or trays have not been opened, return the bioprosthesis in its original packaging.
- Package Opened but Bioprosthesis Not Implanted: If the tray is opened, the bioprosthesis is no longer sterile. If the bioprosthesis is not implanted, it should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde and returned to the company. Refrigeration is not necessary under these circumstances.
- Explanted Bioprosthesis: The explanted bioprosthesis should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde and returned to the company. Refrigeration is not necessary under these circumstances.

11. Safety in the Magnetic Resonance (MR) Environment

MR Conditional

Non-clinical testing has demonstrated that the Edwards Pericardial Mitral Bioprosthesis, Model 11000M is MR Conditional. A patient with the model 11000M bioprosthesis can be scanned safely, immediately after placement of this implant under the following conditions:

- Static magnetic field of 3 tesla or less.
- Maximum Spatial gradient field of 720 gauss/cm.
- Maximum MR system-reported whole-body-averaged specific absorption rate (SAR) of 3W/kg for 15 minutes of scanning.

In non-clinical testing, the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, produced a temperature rise of less than or equal to 0.5 °C at a maximum MR system reported whole-body-averaged specific absorption rate (SAR) of 3W/kg for 15 minutes of MR scanning in a 3 tesla MR system (Excite, Software G3.0-052B, General Electric Healthcare).

MR image quality may be compromised if the area of interest is in the same area or relatively close to the position of the Model 11000M bioprosthesis. Optimization of MR imaging parameters is recommended.

12. Patient Information

12.1 Study Identification Card

A Study Identification Card is provided to each subject implanted with the Edwards Pericardial Mitral Bioprosthesis, Model 11000M.

12.2 Patient Information Materials

Patient information materials may be obtained from Edwards or an Edwards clinical sales specialist.

13. References

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4. Carpentier A. From Valvular Xenograft to Valvular Bioprosthesis (1965-1977). *Med. Instrum*. 1977; 11(2):98-101.
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9. Jamieson,W.R.E., et al. Carpentier-Edwards Standard Porcine Bioprosthesis: Primary Tissue Failure (Structural Valve Deterioration) by Age Groups. *Ann Thorac Surg* 1988, 46:155-162.
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13. Silver, M.M., et al. Calcification in Porcine Xenograft Valves in Children. *Am J. Cardiol* 1980, 45:685-689.
14. Carpentier, A., et al. Continuing Improvements in Valvular Bioprostheses. *J. Thorac Cardiovasc Surg* 1982, 83(1):27-42.

Refer to the symbol legend at the end of this document.

Table 3: Observed Adverse Event Rates for MVR and DVR (Model 6900)

All patients analyzed: N = 363 Cumulative follow-up: 1100 patient-years

	Early Events		Late Events[1]		Freedom from Event (%) [95% CI][2]		
Complication	n[3]	%	n	%/pt.-yr.	1 year (n = 287)	5 years (n = 141)	8 years (n = 18)
Mortality (all)	34	9.4	50	4.7	85.5 [81.8, 89.2]	75.4 [70.3, 80.6]	65.4 [57.6, 73.2]
Valve-related events							
Mortality (valve-related)	0	0	16	1.5	97.7 [96.0, 99.4]	95.3 [92.8, 97.8]	91.9 [87.5, 96.4]
Explants	0	0	8	0.7	98.7 [98.0, 99.3]	96.7 [95.3, 98.0]	95.6 [93.9, 97.3]
Reoperations	2	0.6	12	1.1	97.1 [96.2, 98.1]	95.1 [93.6, 96.6]	93.0 [90.9, 95.1]
Anticoagulant-related hemorrhage	2	0.6	9	0.8	97.1 [95.2, 99.0]	97.1 [95.2, 99.0]	94.1 [88.2, 100]
Endocarditis	1	0.3	3	0.3	99.0 [97.9, 100]	98.7 [97.4, 98.9]	98.7 [97.4, 98.9]
Hemolysis	0	0.0	1	0.1	99.7 [99.0, 100]	99.7 [99.0, 100]	99.7 [99.0, 100]
Nonstructural dysfunction	0	0.0	3	0.3	100 [100, 100]	99.3 [98.0, 100]	98.3 [95.9, 100]
Perivalvular leak (all)	1	0.3	5	0.5	98.4 [97.0, 99.8]	98.4 [97.0, 99.8]	97.3 [94.9, 99.8]
Structural valve deterioration	0	0.0	5	0.5	100.0 [100, 100]	97.6 [95.2, 100]	92.8 [85.3, 100]
Thromboembolism	5	1.4	8	0.7	97.5 [95.8, 99.2]	96.1 [93.8, 98.5]	96.1 [93.8, 98.5]
Thrombosis	0	0.0	0	0.0	100.0 [100, 100]	100.0 [100, 100]	100.0 [100, 100]

Notes:

1. Late event rates were calculated as linearized rates (%/pt-yr) based on 1072.5 late patient-years (> 30 days postoperatively).
2. Freedom from event rates were calculated using the Kaplan-Meier method. Greenwood's formula was used for calculation of the standard errors of these estimates.
3. n = number of events.

Table 4: Observed Adverse Event Rates (Model 6900P)

All patients analyzed: N = 209 Cumulative follow-up: 873.18 total pt-yrs.

	Early Events		Late Events[1]		Freedom from Event (%) [95% CI][2]	
Complication	n[3]	%	n	%/pt-yr	1 year	5 years
Mortality (all)	3	1.4	45	5.3	93.2 [88.8, 95.9]	74.4 [66.9, 80.5]
Valve-related events						
Mortality (valve-related)	1	0.5	12	1.4	98.5 [95.5, 99.5]	92.0 [86.2, 95.5]
Explants	1	0.5	8	0.9	97.5 [94.0, 98.9]	96.5 [92.2, 98.5]
Reoperations	0	0.0	0	0.0	100.0 [100, 100]	100.0 [100, 100]
Bleeding Events	5	2.4	13	1.5	96.1 [92.3, 98.0]	91.9 [86.5, 95.2]
Endocarditis	1	0.5	3	0.4	99.5 [96.6, 99.9]	97.1 [92.1, 98.9]
Nonstructural dysfunction	0	0.0	1	0.1	99.5 [96.4, 99.9]	99.5 [96.4, 99.9]
Perivalvular leak (all)	1	0.5	2	0.2	99.5 [96.7, 99.9]	98.4 [95.2, 99.5]
Structural valve deterioration	0	0.0	2	0.2	100.0 [100, 100]	99.0 [93.2, 99.9]
Thromboembolism	4	1.9	12	1.4	97.0 [93.5, 98.7]	91.3 [85.8, 94.7]
Thrombosis	0	0.0	0	0.0	100.0 [100, 100]	100.0 [100, 100]

Notes:

1. Late event rates were calculated as linearized rates (%/pt-yr) based on 856.24 late patient-years (> 30 days postoperatively).
2. Freedom from event rates were calculated using the Kaplan-Meier method. Greenwood's formula was used for calculation of the standard errors of these estimates.
3. n = number of events.

Table 5: Preoperative Patient Demographics (Model 6900)

Variable	Category	Study Characteristics (N = 363; 1100 total pt-yrs.)	
		n	% (n/N)[1]
Age at implant (N = 363)	Mean ± SD	66.1 ± 10.7	
Gender	Female/Male	212/151	58.4%/41.6%
Diagnosis/Etiology	None	30	8.3%
	Stenosis	91	25.1%
	Regurgitation	184	50.7%
	Mixed Disease	58	16.0%

Note:

1. n = number of patients in each category; N = total number of study patients.

Table 6: Preoperative Patient Demographics (Model 6900P)

Variable	Category	Study Characteristics (N = 209; 873.18 total pt-yrs.)	
		n	% (n/N)[1]
Age at implant (N = 209)	Mean ± SD	71.4 ± 9.4	
Gender	Female/Male	138/71	66.0%/34.0%
Diagnosis/Etiology	Mixed Disease	48	23.0%
	Regurgitation	121	57.9%
	Stenosis	32	15.3%
	Valve Dysfunction	8	3.8%

Note:

1. n = number of patients in each category; N = total number of study patients.

Table 7: Operative Patient Demographics (Model 6900)

		Study Characteristics (N = 363; 1100 total pt-yrs.)	
Variable	Category	n	% (n/N)[1]
Etiology[2]	Rheumatic heart disease	135	37.2%
	Calcification	82	22.6%
	Degeneration	50	13.8%
	Endocarditis	39	10.7%
	Failed Bioprosthesis	15	4.1%
	Ischemic Heart Disease	14	3.9%
	Congenital Abnormalities	8	2.2%
	Other	44	12.1%
Concomitant Procedures[2]	None	200	55.1%
	CABG[3]	78	21.5%
	Tricuspid Repair	61	16.8%
	Intra-aortic balloon pump	17	4.7%
	Pacemaker[4]	6	1.7%
	Aortic repair/replacement	5	1.4%
	Aneurysm Repair	4	1.1%
	Other	31	8.5%
Pre-existing Conditions[2]	None	122	33.6%
	CAD[5]/CABG	72	19.8%
	Hypertension	61	16.8%
	Atrial Fibrillation	53	14.6%
	Previous MI[6]	45	12.4%
	Cerebrovascular Disease	36	9.9%
	Other	234	64.5%
Valve Size (mm)	25	22	6.1%
	27	110	30.3%
	29	137	37.7%
	31	81	22.3%
	33	13	3.6%

Notes:

1. n = number of patients in each category; N = total number of study patients
2. May be more than one per patient
3. CABG = Coronary Artery Bypass Graft
4. Permanent or temporary
5. CAD = Coronary Artery Disease
6. MI = Myocardial Infarction

Table 8: Operative Patient Demographics (Model 6900P)

		Study Characteristics (N = 209; 873.18 total pt-yrs.)	
Variable	Category	n	% (n/N)[1]
Etiology[2]	Calcified	38	18.2%
	Congenital	1	0.5%
	Degenerative	105	50.2%
	Endocarditis Remote	10	4.8%
	Ischemic	12	5.7%
	Rheumatic	64	30.6%
	Other	36	17.2%
Concomitant Procedures[2]	None	91	43.5%
	Aortic Valve/Annulus Repair	3	1.4%
	CABG[3]	58	27.8%
	Permanent Pacemaker	1	0.5%
	Tricuspid Valve/Annulus Repair	21	10.0%
	Other	78	37.3%
Pre-existing Conditions[2]	None	17	8.1%
	Arrhythmias	95	45.5%
	CAD[4]	85	40.7%
	Cardiomyopathy	13	6.2%
	Congestive Heart Failure	66	31.6%
	Endocarditis	14	6.7%
	Myocardial Infarction	21	10.0%
	Peripheral Vascular Disease	9	4.3%
	Pulmonary Hypertension	66	31.6%
	Rheumatic Fever	16	7.7%
	Systemic Hypertension	49	23.4%
	TIA[5]/CVA[6]	24	11.5%
	Other	35	16.7%
Valve Size (mm)	25	28	13.4%
	27	37	17.7%
	29	84	40.2%
	31	43	20.6%
	33	17	8.1%

Notes:

1. n = number of patients in each category; N = total number of study patients
2. May be more than one per patient
3. CABG = Coronary Artery Bypass Graft
4. CAD = Coronary Artery Disease
5. TIA = Transient Ischemic Attack
6. CVA = Cerebral Vascular Accident

Table 9: Effectiveness Outcomes, Functional NYHA (Model 6900)

NYHA Functional Class	Preoperative Assessment		Postoperative Assessments			
			1 to 2 Year		5 Year	
	n/N[1]	%	n/N	%	n/N	%
I	11/363	3.0	120/268	44.8	40/129	31.0
II	73/363	20.1	90/268	33.6	25/129	19.4
III	192/363	52.9	15/268	5.6	1/129	0.8
IV	84/363	23.1	0/268	0.0	0/129	0.0
Not Available	3/363	0.8	43/268	16.0	63/129	48.8

Note:

1. n = number of patients in each category; N = total number of study patients.

Table 10: Effectiveness Outcomes, Functional NYHA (Model 6900P)

NYHA Functional Class	Preoperative Assessment		Postoperative Assessments			
			1 Year		5 Year	
	n/N[1]	%	n/N	%	n/N	%
I	6/209	2.9	86/187	46.0	30/96	31.3
II	27/209	12.9	68/187	36.4	33/96	34.4
III	121/209	57.9	8/187	4.3	6/96	6.3
IV	55/209	26.3	1/187	0.5	0/96	0.0
Not Available	0/209	0.0	24/187	12.8	27/96	28.1

Note:

1. n = number of patients in each category; N = total number of study patients.

Table 11: Effective Outcomes, Hemodynamic Results[1] (Model 6900)

Hemodynamic Parameter	Results By Valve Size				
	25 mm	27 mm	29 mm	31 mm	33 mm
Discharge/Early Post-Implant (n = 130, 109 MVR[2] and 21 DVR[3])					
Mean gradient[4]	n = 3	n = 23	n = 36	n = 23	n = 3
• mean ± sd	5.7 ± 1.2	4.2 ± 1.7	4.2 ± 1.7	3.6 ± 1.0	7.5 ± 5.8
• min, max	5, 7	2, 9	1, 8	2, 5	3, 14
EOA[5]	n = 1	n = 17	n = 22	n = 25	n = 5
• mean ± sd	1.5	2.9 ± 0.9	3.1 ± 0.9	2.5 ± 0.7	3.0 ± 1.2
• min, max	1.5, 1.5	1.3, 4.1	1.4, 4.2	1.5, 3.8	1.6, 4.9
Regurgitation[6]	n = 3	n = 28	n = 51	n = 40	n = 8
0	3/3 (100%)	22/28 (79%)	36/51 (71%)	30/40 (75%)	4/8 (50%)
1+	0/3 (0%)	5/28 (18%)	13/51 (25%)	7/40 (18%)	4/8 (50%)
2+	0/3 (0%)	0/28 (0%)	1/51 (2%)	3/40 (7%)	0/8 (0%)
3+	0/3 (0%)	0/28 (0%)	1/51 (2%)	0/40 (0%)	0/8 (0%)
4+	0/3 (0%)	0/28 (0%)	0/51 (0%)	0/40 (0%)	0/8 (0%)
Not available	0/3 (0%)	1/28 (3%)	0/51 (0%)	0/40 (0%)	0/8 (0%)
3 to 6 Month Post-Implant Interval (n = 49, 42 MVR[2] and 7 DVR[3])					
Mean gradient[4]	n = 5	n = 19	n = 15	n = 5	n = 2
• mean ± sd	6.4 ± 1.7	5.3 ± 5	3.4 ± 1.2	4 ± 1.9	4 ± 0
• min, max	5, 9	2, 25	2, 6	2, 7	4, 4
EOA[5]	n = 5	n = 18	n = 13	n = 5	n = 2
• mean ± sd	2.9 ± 0.8	2.6 ± 0.7	2.8 ± 0.6	2.9 ± 0.3	2.6 ± 1
• min, max	1.8, 3.6	1.5, 5	2, 3.8	2.4, 3.3	2, 3.3
Regurgitation[6]	n = 5	n = 21	n = 15	n = 6	n = 2
0	3/5 (60%)	17/21 (81%)	6/15 (40%)	4/6 (67%)	1/2 (50%)
1+	0/5 (0%)	4/21 (19%)	8/15 (53%)	2/6 (33%)	0/2 (0%)
2+	1/5 (20%)	0/21 (0%)	1/15 (7%)	0/6 (0%)	1/2 (50%)
3+	0/5 (0%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)
4+	1/5 (20%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)
Not available	0/5 (0%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)

Continued on following page.

Table 11: Effective Outcomes, Hemodynamic Results[1] (Model 6900), Continued

Hemodynamic Parameter	Results By Valve Size				
	25 mm	27 mm	29 mm	31 mm	33 mm
1 to 2 Year Post-Implant Interval (n = 131, 114 MVR[2] and 17 DVR[3])					
Mean gradient[4]	n = 3	n = 40	n = 47	n = 27	n = 4
• mean ± sd	5.2 ± 0.7	4.1 ± 1.6	3.5 ± 1.8	3.1 ± 1.4	2.1 ± 0.5
• min, max	4.7, 6	1, 7	1, 10	1, 7	1.5, 2.7
EOA[5]	n = 2	n = 35	n = 46	n = 29	n = 5
• mean ± sd	1.8 ± 0.4	2.3 ± 0.6	2.6 ± 0.5	2.6 ± 0.7	2.5 ± 0.5
• min, max	1.5, 2.0	1.2, 3.5	1.1, 3.7	1.1, 3.7	2.1, 3.2
Regurgitation[6]	n = 4	n = 42	n = 51	n = 29	n = 5
0	2/4 (50%)	31/42 (74%)	36/51 (71%)	17/29 (59%)	3/5 (60%)
1+	1/4 (25%)	9/42 (21%)	11/51 (21%)	8/29 (27%)	1/5 (20%)
2+	1/4 (25%)	2/42 (5%)	4/51 (8%)	2/29 (7%)	1/5 (20%)
3+	0/4 (0%)	0/42 (0%)	0/51 (0%)	2/29 (7%)	0/5 (0%)
4+	0/4 (0%)	0/42 (0%)	0/51 (0%)	0/29 (0%)	0/5 (0%)
Not available	0/4 (0%)	0/42 (0%)	0/51 (0%)	0/29 (0%)	0/5 (0%)
5 Year Post-Implant Interval (n = 11, 9 MVR[2] and 2 DVR[3])					
Mean gradient[4]	n = 0	n = 6	n = 5	n = 0	n = 0
• mean ± sd	N/A	8.8 ± 8.1	5.1 ± 2.3	N/A	N/A
• min, max	N/A	4, 25	3, 8	N/A	N/A
EOA[5]	n = 0	n = 2	n = 4	n = 0	n = 0
• mean ± sd	N/A	2.0 ± 1.5	2.9 ± 0.6	N/A	N/A
• min, max	N/A	1.0, 3.1	2.1, 3.5	N/A	N/A
Regurgitation[6]	n = 0	n = 6	n = 5	n = 0	n = 0
0	0/0 (0%)	4/6 (66%)	2/5 (40%)	0/0 (0%)	0/0 (0%)
1+	0/0 (0%)	1/6 (17%)	3/5 (60%)	0/0 (0%)	0/0 (0%)
2+	0/0 (0%)	1/6 (17%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
3+	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
4+	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
Not available	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)

Notes:

1. Hemodynamic evaluations were performed using transthoracic echocardiography (TTE) and in some cases, transesophageal echocardiography (TEE).
2. MVR = mitral valve replacement
3. DVR = double valve replacement
4. Mean gradient in mmHg
5. EOA: Effective Orifice Area, cm^2
6. Regurgitation = none, 0; mild, 1+; moderate, 2+; moderate/severe, 3+; severe, 4+

Table 12: Effectiveness Outcomes, Hemodynamic Results (Model 6900P)[1]

Hemodynamic Parameter	Results By Valve Size				
	25 mm	27 mm	29 mm	31 mm	33 mm
Discharge/Early Post-Implant					
Mean gradient[2]	n = 24	n = 35	n = 83	n = 42	n = 16
• mean ± sd	6.4 ± 1.87	4.4 ± 1.52	3.4 ± 1.47	3.3 ± 1.20	4.0 ± 1.38
• min, max	3, 10	1.96, 8	1.4, 9	1, 7	1.5, 6.91
EOA[3]	n = 8	n = 27	n = 77	n = 41	n = 16
• mean ± sd	2.7 ± 0.87	2.8 ± 0.58	2.9 ± 0.93	2.5 ± 0.67	2.4 ± 0.52
• min, max	1.46, 4.4	1.5, 3.9	1.58, 6	1.32, 4.2	1.55, 3.31
Regurgitation[4]	n = 27	n = 37	n = 83	n = 43	n = 17
Trivial / None	19/27 (70%)	29/37 (78%)	76/83 (92%)	39/43 (91%)	15/17 (88%)
1+ Mild	6/27 (22%)	7/37 (19%)	7/83 (8%)	4/43 (9%)	1/17 (6%)
2+ Moderate	1/27 (4%)	1/37 (3%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
3+ Moderate/Severe	0/27 (0%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	1/17 (6%)
4+ Severe	0/27 (0%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
Not available	1/27 (4%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
3 to 6 Month Post-Implant Interval					
Mean gradient[2]	n = 0	n = 4	n = 3	n = 2	n = 0
• mean ± sd	0 ± 0	4.4 ± 2.25	2.3 ± 0.89	6.6 ± 2.05	0 ± 0
• min, max	0, 0	2.5, 7.5	1.3, 3	5.1, 8	0, 0
EOA[3]	n = 0	n = 3	n = 3	n = 1	n = 1
• mean ± sd	0 ± 0	2.4 ± 0.74	3.2 ± 0.88	2.5 ± 0.00	1.2 ± 0.00
• min, max	0, 0	1.6, 3	2.3, 4.05	2.47, 2.47	1.22, 1.22
Regurgitation[4]	n = 0	n = 5	n = 3	n = 2	n = 2
Trivial / None	0	3/5 (60%)	2/3 (67%)	2/2 (100%)	2/2 (100%)
1+ Mild	0	1/5 (20%)	1/3 (33%)	0/2 (0%)	0/2 (0%)
2+ Moderate	0	1/5 (20%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
3+ Moderate/Severe	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
4+ Severe	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
Not available	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)

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Table 12: Effectiveness Outcomes, Hemodynamic Results (Model 6900P)[1], Continued

Hemodynamic Parameter	Results By Valve Size				
	25 mm	27 mm	29 mm	31 mm	33 mm
1 Year Post-Implant Interval					
Mean gradient[2]	n = 16	n = 27	n = 63	n = 34	n = 15
• mean ± sd	5.9 ± 2.36	4.0 ± 1.45	3.0 ± 1.61	3.3 ± 1.26	3.4 ± 1.25
• min, max	3, 12	2, 7	1, 12	1.5, 7	1.9, 6.3
EOA[3]	n = 3	n = 21	n = 59	n = 32	n = 15
• mean ± sd	2.3 ± 0.16	2.4 ± 0.76	2.6 ± 0.74	2.5 ± 0.67	2.3 ± 0.83
• min, max	2.09, 2.4	1.27, 4.76	1.5, 5.7	1.5, 4	1.2, 3.8
Regurgitation[4]	n = 20	n = 28	n = 65	n = 34	n = 16
Trivial / None	17/20 (85%)	24/28 (86%)	53/65 (82%)	29/34 (85%)	13/16 (81%)
1+ Mild	3/20 (15%)	3/28 (11%)	6/65 (9%)	3/34 (9%)	3/16 (19%)
2+ Moderate	0/20 (0%)	0/28 (0%)	3/65 (5%)	2/34 (6%)	0/16 (0%)
3+ Moderate/Severe	0/20 (0%)	0/28 (0%)	1/65 (2%)	0/34 (0%)	0/16 (0%)
4+ Severe	0/20 (0%)	0/28 (0%)	0/65 (0%)	0/34 (0%)	0/16 (0%)
Not available	0/20 (0%)	1/28 (4%)	2/65 (3%)	0/34 (0%)	0/16 (0%)

Notes:

1. Hemodynamic evaluations were performed using transthoracic echocardiography (TTE) and in some cases, transesophageal echocardiography (TEE).
2. Mean gradient in mmHg
3. EOA: Effective Orifice Area, cm^2
4. Regurgitation = Trivial/none, 0; mild, 1+; moderate, 2+; moderate/severe, 3+; severe, 4+

Français

Bioprothèse mitrale péricardique d'Edwards, modèle 11000M

Mode d'emploi

ATTENTION : dispositif expérimental. Limité à une utilisation expérimentale en vertu des lois fédérales (États-Unis).

AVERTISSEMENT : dispositif expérimental. Exclusivement à des fins de recherche clinique.

Avertissement : dispositif expérimental. Utilisation limitée à la recherche. Pour une utilisation par des (médecins) chercheurs qualifiés uniquement.

1. Description du dispositif et des accessoires

1.1 Description du dispositif

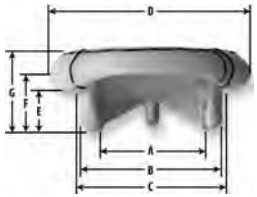
La bioprothèse mitrale péricardique d'Edwards, modèle 11000M, est une bioprothèse trivalve composée d'un péricarde bovin traité installé sur une structure flexible. Elle est disponible dans les tailles suivantes : 25, 27, 29, 31 et 33 mm (tableau 1). Elle est conservée dans un emballage non aqueux et ne nécessite pas de rinçage avant l'implantation.

Le fil métallique est fait d'un alliage de chrome-cobalt recouvert d'un matériau tissé en polyester. Une bande laminée en alliage de chrome-cobalt et film en polyester entoure la base de la structure en fil métallique.

Un anneau de suture gaufré en silicone, qui est couvert d'un tissu poreux en polytétrafluoroéthylène (PTFE), est attaché à la structure en fil métallique. L'anneau de suture est crénelé sur sa partie antérieure. Les marqueurs de suture en soie noire de la partie antérieure contribuent à orienter la bioprothèse et à éviter que la voie d'évacuation du ventricule droite ne soit obstruée par un montant.

L'anneau de suture est encerclé par une ligne de guidage de suture en soie noire. L'utilisation de cette ligne pour positionner les sutures à travers l'anneau de suture et dans la région sur la partie externe de l'anneau de suture facilite la pénétration de l'aiguille et donne une compliance variable. Les cellules du gaufrage sont plus larges dans la partie postérieure, là où les calcifications et les irrégularités de l'anneau mitral d'origine sont plus fréquentes (réf. 6).

Tableau 1. Dimensions nominales



HVT63

Taille	25 mm	27 mm	29 mm	31 mm	33 mm
A. Diamètre de l'endoprothèse (fil métallique, mm)	25	27	29	31	31
B. Diamètre de l'anneau tissulaire (mm)	28	29,5	31,5	33,5	33,5
C. Diamètre du montant de l'endoprothèse externe (embout, mm)	29	31	34	35	35
D. Diamètre de l'anneau de suture externe (en mm)	36	38	40	42	44
E. Profil effectif antérieur (mm)	7	7,5	8	8,5	8,5
F. Profil effectifpostérieur (mm)	10	10,5	11	11,5	11,5
G. Hauteur profil total (mm)	15	16	17	18	18
Surface de l'orifice (en mm^2)	424	499	580	653	653

1.2 Description des accessoires

Les accessoires pouvant être utilisés avec la bioprothèse 11000M sont les suivants :

- Système de support Tricentrix
- Calibreur pour réplique 1173R
- Calibreur pour porteuse 1173B
- Plateau de stérilisation fourni avec le modèle SET1173
- Modèles de poignée 1111, 1117, 1173 et 1126 (pour utilisation unique)

Tous les accessoires sont vendus non stériles, sauf le système de support Tricentrix qui est fixé à la bioprothèse stérile et la poignée 1126 qui est réservée à une utilisation unique.

Calibreurs et plateau

Seuls les calibreurs 1173B (figure 1a) et 1173R (figure 1b) peuvent être employés avec la bioprothèse 11000M.

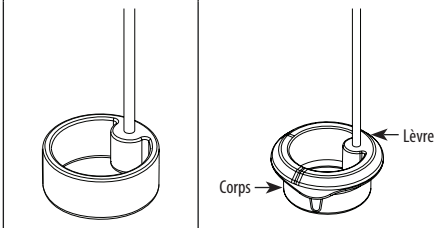
Attention : pour calibrer la bioprothèse 11000M, ne pas utiliser de calibreurs de valves d'autres fabricants ou d'autres prothèses de valves d'Edwards Lifesciences.

N'utiliser que les calibreurs 1173B ou 1173R pour définir la taille à employer pour la bioprothèse 11000M. Les calibreurs 1173B et 1173R permettent de constater immédiatement si la prothèse s'adapte à l'anneau et sont proposés pour chaque taille de bioprothèse 11000M. Le corps des calibreurs 1173B et 1173R indique le diamètre de l'endoprothèse à la base. Grâce à sa partie antérieure crénelée et à ses marqueurs noirs, la lèvre du calibreur 1173R reproduit l'anneau de suture de

la bioprothèse et permet de déterminer les résultats de la suture ou des techniques de préservation de l'appareil sous-valvulaire.

Les calibreurs 1173B et 1173R portent une étiquette indiquant la taille de la bioprothèse. La trousse complète de calibreurs se trouve dans un plateau, modèle SET1173, qui peut être réutilisé et restérilisé.

Figure 1a – Calibreur pour porteuse 1173B	Figure 1b – Calibreur pour réplique 1173R
CP1089-16	CP1089-15

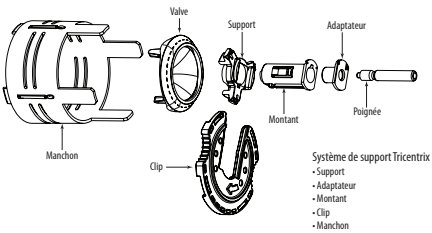


Système de support Tricentrix et poignées

L'ensemble de poignée et support est constitué de deux composants : le système de support Tricentrix (figure 2) monté sur la bioprothèse 11000M, et une poignée (1111, 1117, 1173 ou 1126) fixée au système de support Tricentrix lors de l'opération chirurgicale.

Figure 2 – Système de support Tricentrix

CP1089-28



HVT55

Les poignées suivantes (tableau 2) peuvent être utilisées avec la bioprothèse 11000M.

Tableau 2. Poignées accessoires

Modèle	Matériau de l'axe	Longueur totale		Réutilisable
		pouces	cm	
1111	Acier inoxydable	7,0	17,8	Oui
1117	Nitinol	9,1	23,2	Oui
1126	Acier inoxydable	11,5	29,2	Non
1173	Nitinol	11,3	28,6	Oui

Les poignées équipées d'un axe en nitinol sont plus souples que celles en acier inoxydable. Lors de chaque cycle de stérilisation, elles redeviennent droites, ce qui facilite leur fixation au support.

2. Mode d'emploi

La bioprothèse mitrale péricardique d'Edwards, modèle 11000M, est destinée aux patients dont il faut remplacer la valve mitrale d'origine ou prothétique.

3. Contre-indications

Ne pas utiliser la bioprothèse si le chirurgien estime que son utilisation est contraire à l'intérêt du patient. La décision finale à ce propos relève du chirurgien qui doit évaluer tous les risques impliqués, y compris l'anatomie et la pathologie observées au moment de l'opération chirurgicale.

4. Mises en garde

POUR UTILISATION UNIQUE SEULEMENT. Ce dispositif est conçu, destiné et distribué pour une utilisation unique seulement. Ne pas restériliser ou réutiliser ce dispositif. Aucune donnée n'existe pour corroborer le caractère stérile, la non-pyrogénicité et la fonctionnalité du dispositif après le processus de restérilisation. La bioprothèse et l'emballage deviendront inutilisables en cas d'exposition à des radiations, à la vapeur, à l'oxyde d'éthylène ou à d'autres agents chimiques de stérilisation.

NE PAS CONGELER NI EXPOSER LA BIOPROTHÈSE À UNE CHALEUR EXTRÊME. L'exposition de la bioprothèse à des températures extrêmes rendra le dispositif inutilisable.

NE PAS UTILISER la bioprothèse :

- **si le sachet métallisé, les plateaux scellés ou les lèvres sont ouverts, endommagés ou tachés ;**
- **si la date d'expiration est passée ;**
- **si elle est tombée, endommagée ou mal manipulée de quelle que façon que ce soit. Si une bioprothèse est endommagée lors de l'insertion, ne pas tenter de la réparer.**

NE PAS EXPOSER la bioprothèse à des solutions, des produits chimiques, des antibiotiques, etc., à l'exception de solutions salines physiologiques. Le tissu de la valve peut comporter des dommages irréparables non apparents lors d'une inspection visuelle.

NE PAS SAISIR le tissu de la valve de la bioprothèse avec des instruments ni endommager la bioprothèse. Même la plus petite perforation du tissu de la valve peut s'agrandir à terme et compromettre gravement son fonctionnement.

NE PAS CHOISIR UNE TAILLE SUPÉRIEURE. Le choix d'une taille supérieure peut entraîner des dommages à la bioprothèse ou un stress mécanique localisé, susceptible de blesser le cœur ou de causer une panne du tissu de la valve, une distorsion de l'endoprothèse ou une régurgitation du tissu de la valve.

NE PAS PASSER, à travers la bioprothèse, des cathéters, des sondes électrodes transveineuses ou d'autres instruments chirurgicaux autres qu'un miroir servant à vérifier le positionnement des montants et des sutures. Les autres dispositifs risquent d'endommager le tissu de la valve.

Comme pour tout dispositif médical implanté, il existe un risque de réponse d'immunisation de la part du patient. Certains composants du modèle 11000M sont en alliage contenant du cobalt, du chrome, du nickel, du molybdène, du manganèse, du carbone, du béryllium et du fer. Il faut prendre des précautions avec les patients souffrant d'hypersensibilité à ces matières. Ce dispositif ne contient pas de latex mais peut avoir été fabriqué dans un environnement qui en contient.

5. Évènements indésirables

5.1 Évènements indésirables observés

Comme pour toutes les valves cardiaques prothétiques, des évènements indésirables graves pouvant parfois aller jusqu'au décès peuvent survenir. En outre, des évènements indésirables découlant de la réaction du patient au dispositif implanté ou encore d'une modification physique ou chimique de ses composants, plus particulièrement de ceux dont l'origine est biologique, peuvent survenir à des intervalles variables (allant de plusieurs heures à plusieurs jours) et nécessitent une nouvelle opération pour remplacer la prothèse.

La conception de la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, est similaire à celle des bioprothèses péricardiques PERIMOUNT Magna Mitral Ease du modèle 7300TFX de Carpentier-Edwards.

Trois (3) essais cliniques multicentre prospectifs non randomisés ont été effectués hors des États-Unis avec la bioprothèse mitrale péricardique 6900. Sur l'ensemble des patients, trois cent un (301) ont subi un remplacement isolé de la valve mitrale (RVM) tandis que 62 subissaient un double remplacement valvulaire (DRV), la valve aortique étant remplacée par une bioprothèse aortique péricardique PERIMOUNT de Carpentier-Edwards.

Les bioprothèses ont été implantées de 1984 à 1986 dans la première étude, de 1989 à 1994 dans la deuxième et de 1996 à 1997 dans la troisième. Les patients ont été évalués avant l'opération, pendant l'opération, à la sortie, après 1 an et tous les ans par la suite.

Le tableau 3 présente les taux observés d'évènements précoces (≤ 30 jours pour les évènements indésirables en lien avec la valve), le taux linéarisé pour les évènements tardifs (> 30 jours postopératoires) et les taux actuariels d'évènements indésirables 1, 5 et 8 ans après l'opération pour le modèle 6900. Les taux d'évènements indésirables concernaient 363 patients de neuf centres. Le suivi cumulatif était de 1 100 patient-années, avec une moyenne de suivi de 3 années (écart-type = 2,4 années, intervalle = 0 à 8,2 ans). Les données démographiques des patients en période préopératoire et opératoire sont présentées dans les tableaux 5 et 7. Les résultats en matière d'efficacité sont présentés dans les tableaux 9 et 11.

Un (1) essai clinique multicentre prospectif non randomisé a été effectué à l'échelon international auprès de patients ayant reçu la bioprothèse mitrale péricardique PERIMOUNT 6900P de Carpentier-Edwards. Sur l'ensemble des patients, cent soixante-quinze (175) ont subi un remplacement isolé de la valve mitrale (RVM) tandis que trente-quatre (34) subissaient un double remplacement (DRV), la valve aortique étant remplacée par une bioprothèse aortique péricardique PERIMOUNT de Carpentier-Edwards. Dans cette étude, les bioprothèses ont été implantées de 1999 à 2007. Les patients étaient évalués pendant la période préopératoire, pendant la période péropératoire et à la sortie, après 1 an et chaque année par la suite. Les évènements indésirables ont été consignés tout au long de la période postopératoire. Le tableau 4 présente les taux observés d'évènements précoces (≤ 30 jours pour les évènements indésirables en lien avec la valve), le taux linéarisé pour les évènements tardifs (> 30 jours postopératoires) et les taux actuariels d'évènements indésirables 1 et 5 ans après l'opération pour le modèle 6900P. Les taux d'évènements indésirables concernaient deux cent neuf (209) patients de sept centres. Le suivi cumulatif était de 873,18 patient-années, avec une moyenne de suivi de 4,2 années (écart-type = 2,3 années, intervalle = 0 à 8,2 ans). Les données démographiques des patients en période préopératoire et opératoire sont présentées dans les tableaux 6 et 8. Les résultats en matière d'efficacité sont présentés dans les tableaux 10 et 12.

5.2 Évènements indésirables potentiels

Les évènements indésirables potentiels associés à l'utilisation de biovalves cardiaques prothétiques sont les suivants :

- Angine de poitrine
- Diathèse hémorragique (coagulopathie) en lien avec l'anticoagulothérapie
- Arythmie cardiaque
- Blocage de la valve ostiale coronaire
- Endocardite
- Insuffisance cardiaque
- Hémolyse
- Anémie hémolytique
- Hémorragie
- Infection locale et systémique
- Infarctus du myocarde
- Inadaptation de la prothèse au patient
- Enclavement de la valve prothétique (coincement)
- Dysfonction non structurelle de la prothèse
- Pannus de la prothèse
- Fuite périvalvulaire de la prothèse
- Régurgitation de la prothèse
- Détérioration de la structure de la prothèse
- Thrombose prothétique
- Accident vasculaire cérébral
- Thrombo-embolie
- Insuffisance cardiaque congestive

Ces complications peuvent avoir les conséquences suivantes :

- Nouvelle opération chirurgicale
- Explantation
- Handicap permanent
- Décès

Voici les autres évènements indésirables en lien avec l'utilisation des bioprothèses mitrales péricardiques PERIMOUNT 6900 de Carpentier-Edwards tirés de la documentation et des rapports issus du système de gestion des

plaintes d'Edwards Lifesciences : sténose, régurgitation par une valve insuffisante, perforation du ventricule par les montants de l'endoprothèse, dysfonction de la valve découlant d'une déformation de l'implant et rupture de la structure métallique.

6. Études cliniques

Les indicateurs de sécurité mentionnés dans les études prospectives correspondent aux évènements indésirables. Des analyses sanguines ont été utilisées pour confirmer l'absence ou la présence de certains évènements indésirables. Les résultats concernant la sécurité sont détaillés dans le tableau 3 pour le modèle 6900 et dans le tableau 4 pour le modèle 6900P. Les données démographiques préopératoires sont détaillées dans le tableau 5 pour le modèle 6900 et dans le tableau 6 pour le modèle 6900P. Les données démographiques opératoires sont détaillées dans le tableau 7 pour le modèle 6900 et dans le tableau 8 pour le modèle 6900P. Les indicateurs d'efficacité correspondent à la classification fonctionnelle de la New York Heart Association (NYHA), résumée dans le tableau 9 pour le modèle 6900 et dans le tableau 10 pour le modèle 6900P, et aux évaluations échocardiographiques résumées dans le tableau 11 pour le modèle 6900 et dans le tableau 12 pour le modèle 6900P.

Il n'existe aucune donnée clinique démontrant la résistance accrue à la calcification de la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, par rapport aux autres bioprothèses du marché.

7. Individualisation du traitement

Sauf indication contraire, les destinataires de la valve bioprothétique doivent suivre une anticoagulothérapie pendant les premiers stades suivant l'implantation, selon les consignes données à chacun par le médecin. Une anticoagulothérapie ou un traitement antiplaquettaire à long terme doit être envisagé pour les patients montrant des facteurs de risque de thrombo-embolie.

Le jugement final concernant les soins pour un patient donné doit être pris par le fournisseur de santé et le patient à la lumière de l'ensemble de la situation que présente ce dernier (réf. 7). Il est recommandé de poser une bioprothèse en cas de RVA sur des patients de tous âges qui ne prennent pas de warfarine ou pour lesquels il existe une contre-indication importante à la thérapie à base de warfarine. Les préférences du patient sont également à prendre en compte dans une mesure raisonnable lors du choix de l'opération de la valve mitrale et de la valve prothétique. Il est raisonnable d'envisager l'implantation d'une prothèse mécanique pour un RVA de patients de moins de 65 ans pour lesquels l'anticoagulation n'est pas contre-indiquée. Il est également raisonnable d'envisager l'implantation d'une bioprothèse pour un RVA de patients de moins de 65 ans qui ont fait ce choix pour des raisons de mode de vie après avoir été informés dans les détails des risques de l'anticoagulation par rapport à l'éventuelle nécessité d'un deuxième RVA (réf. 7).

7.1 Populations de patients spécifiques

L'innocuité et l'efficacité de la bioprothèse, modèle 11000M, n'ont pas été établies pour les populations suivantes, sur lesquelles elles n'ont pas été étudiées :

- patientes enceintes ;
- mères qui allaitent ;
- patients métabolisant le calcium de manière anormale (p. ex., insuffisance rénale, hyperparathyroïdisme) ;
- patients présentant une insuffisance dégénérative anévrismale de l'aorte (p. ex., nécrose médiale kystique, syndrome de Marfan) ;
- enfants, adolescents et jeunes adultes.

Attention : Selon des rapports issus de documentation sur des valves tissulaires (réf. 9, 10, 11, 12 et 13), la fréquence des calcifications de la valve serait supérieure chez les patients de moins de 20 ans. Lorsque cela est possible, il faut éviter les injections intraveineuses répétées contenant du calcium pendant la période postopératoire. Parallèlement, la consommation excessive de lait ou de produits laitiers doit être évitée chez l'enfant. À cet égard, les recherches effectuées sur les animaux (réf. 14) démontrent qu'un niveau élevé de calcium dans le système peut entraîner une calcification précoce.

8. Informations et conseils au patient

Il est conseillé de procéder à un suivi sérieux et continu (au moins par une visite annuelle chez le médecin) afin que les complications liées à la bioprothèse, et plus particulièrement aux problèmes de matériau, puissent faire l'objet d'un diagnostic et d'un traitement adaptés. Les patients porteurs de bioprothèses sont vulnérables à la bactériémie (p. ex., lors de procédures dentaires) et doivent recevoir des conseils concernant l'antibioprophylaxie. Enfin, il faut encourager les patients à porter en permanence leur carte d'identification et à informer les fournisseurs dont ils sollicitent des soins qu'ils possèdent un implant.

9. Présentation

9.1 Conditionnement

La bioprothèse mitrale péricardique d'Edwards, modèle 11000M, est stérile et non pyrogène. Elle est livrée dans un emballage de plateau à double barrière placé dans un sachet métallisé, se trouvant lui-même dans un carton.

Chaque bioprothèse se trouve dans un carton avec un indicateur de température visible à travers une fenêtre sur le panneau latéral. Cet indicateur vise à repérer les produits exposés à des températures extrêmes transitoires. À la réception de la bioprothèse, inspecter immédiatement l'indicateur et consulter l'étiquette du carton pour confirmer l'état « Utiliser ». Si l'état « Utiliser » n'est pas apparent, ne pas se servir de la bioprothèse et contacter le fournisseur local ou le représentant d'Edwards Lifesciences pour organiser une autorisation de retour et un remplacement.

Mise en garde : inspecter soigneusement la bioprothèse avant l'implantation pour trouver des traces d'exposition à des températures extrêmes ou d'autres dégâts.

9.2 Stockage

La bioprothèse mitrale péricardique d'Edwards, modèle 11000M, doit être entreposée à une température comprise entre 10 °C et 25 °C (50 °F et 77 °F), dans son sachet métallisé et son carton de rangement.

10. Directives d'utilisation

10.1 Formation du médecin

Les techniques d'implantation de cette bioprothèse sont semblables à celles du placement d'une bioprothèse mitrale avec endoprothèse. Aucune formation particulière n'est nécessaire pour implanter la bioprothèse mitrale péricardique d'Edwards, modèle 11000M.

10.2 Choix de la taille

Attention : pour calibrer la bioprothèse 11000M, ne pas utiliser de calibreurs de valves d'autres fabricants ou d'autres prothèses de valves d'Edwards Lifesciences.

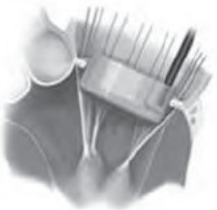
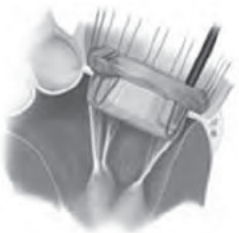
Attention : vérifier si les calibreurs et les poignées contiennent des traces d'usure comme des ternissures, des fissurations ou des craquelures. Remplacer le calibreur ou la poignée en cas de détériorations.

Mise en garde : les fragments des poignées et des calibreurs ne sont pas radio-opaques et ne peuvent pas être détectés par un imageur externe.

Vérifier que les accessoires ont été stérilisés conformément aux recommandations fournies avec les articles réutilisables.

Les marques noires sur la lèvre reproduisent les marqueurs noirs de l'anneau de suture. Elles délimitent la partie antérieure de l'anneau de suture de la bioprothèse, qui doit être positionnée en face de la partie de l'anneau d'origine située entre les commissures de manière à enjamber la région de la voie d'évacuation du ventricule gauche. Sur le calibreur pour la réplique 1173R, la hauteur et l'emplacement des montants de l'endoprothèse sont marqués de manière à faciliter l'alignement et le bon positionnement.

Les calibreurs sont équipés de poignées déjà fixées dont la longueur est augmentée pour un meilleur accès en cas d'exposition difficile, pour les patients ayant une cage thoracique profonde et pour permettre une procédure moins invasive. La manière dont l'arrière de la poignée est fixée au calibreur permet d'avoir une vue dégagée du ventricule à travers le corps afin de mieux évaluer les structures sous-valvulaires. Les calibreurs 1173B et 1173R portent une étiquette indiquant la taille de la bioprothèse.

Étape	Procédure
1	**Choix de la taille à l'aide du calibreur pour porteuse 1173B :** Pour choisir la taille à l'aide du calibreur pour porteuse 1173B, passer son corps à travers l'anneau mitral. Vérifier qu'il repose directement sur la partie plane de l'anneau. HVT60 
2	**Choix de la taille à l'aide du calibreur pour réplique 1173R :** Pour choisir la taille à l'aide du calibreur pour réplique 1173R, passer son corps à travers l'anneau mitral de manière à ce que l'embout du calibreur, qui reproduit l'anneau de suture de la bioprothèse, repose sur la partie supérieure de l'anneau mitral. HVT61 

Certaines techniques, comme l'utilisation de petites compresses, l'enroulement de la valve ou la préservation de l'appareil mitral sous-valvulaire peuvent également réduire la taille de l'anneau mitral et permettre le choix d'une bioprothèse plus petite (réf. 8). Lors de l'utilisation de ces techniques, il est conseillé de réviser la taille de l'anneau pour éviter de choisir une bioprothèse trop grande. Le rendement constant des bioprothèse mitrales péricardiques d'Edwards, modèle 11000M, évite de devoir choisir une taille supérieure pour obtenir le rendement hémodynamique recherché chez la plupart des patients (tableaux 11 et 12).

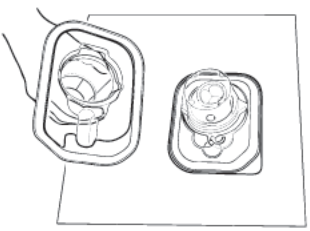
Il peut arriver que la membrure, qui est élastique, soit étirée par le système de support Tricentrix au cours de l'implantation. Elle se rétractera alors autour du montant lorsque le support sera retiré, coinçant ainsi les valves et gênant leur fonctionnement. Les calibreurs 1173B et 1173R sont faits d'un matériau transparent qui permet de voir l'appareil sous-valvulaire au cours du choix de la taille. Veiller à ce qu'aucune membrane ne gêne le passage des montants.

Attention : faire preuve d'une attention toute particulière lors du recours à des techniques de préservation de l'appareil sous-valvulaire, afin d'éviter que la membrane ne se coince dans un montant.

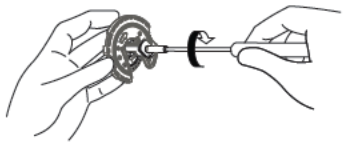
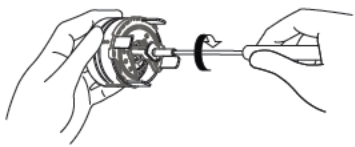
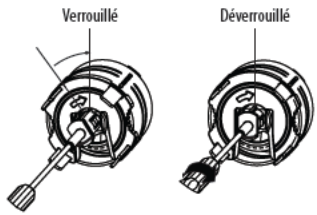
Mise en garde : éviter de choisir une bioprothèse trop grande. Le choix d'une taille supérieure peut entraîner des dommages à la bioprothèse ou un stress mécanique localisé, susceptible de blesser le cœur ou de causer une panne du tissu de la valve, une distorsion de l'endoprothèse ou une régurgitation du tissu de la valve.

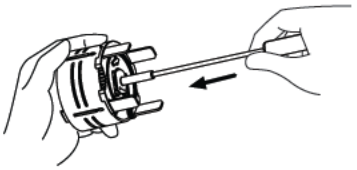
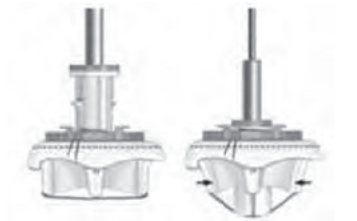
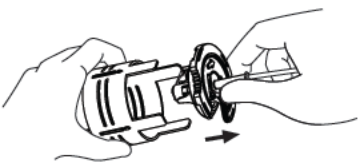
10.3 Instructions de manipulation et de préparation

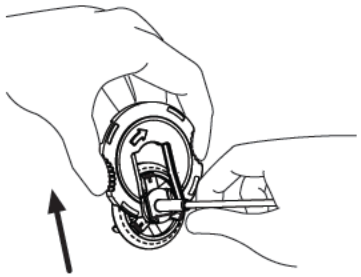
Il est conseillé de suivre une formation sur le tas avant de manipuler et de préparer la bioprothèse mitrale péricardique d'Edwards, modèle 11000M.

Étape	Procédure
1	**Attention : ne pas ouvrir pas l'emballage de la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, avant d'avoir l'assurance que l'implantation aura lieu.** **Mise en garde : Ne pas ouvrir le sachet métallisé dans une zone stérile. Ce sachet ne sert qu'à protéger la bioprothèse. Seul l'emballage le plus à l'intérieur peut pénétrer dans la zone stérile.** Une fois que la bonne taille de bioprothèse a été choisie, retirer le sachet métallisé du carton dans la zone non stérile. Avant d'ouvrir, examiner l'emballage pour vérifier s'il y a des dommages et des scellés cassés ou manquants.
2	Près de la zone stérile, tenir la base du plateau extérieur et retirer son couvercle.
3	Le plateau intérieur et son contenu sont stériles. Transférer le plateau interne sur la zone stérile. Il faut manipuler le contenu du plateau intérieur en recourant à une technique chirurgicale stérile afin d'éviter la contamination. HVT26 

Étape	Procédure
4	**Attention : ne pas ouvrir pas l'emballage intérieur avant d'avoir l'assurance que l'implantation aura lieu et que le chirurgien est prêt à mettre la valve en place.** **Attention : la bioprothèse n'est pas fixée sur le plateau intérieur. Il faut faire attention en ouvrant le couvercle et en tirant sur le couvercle en plastique.** Avant d'ouvrir, examiner le plateau intérieur et le couvercle pour vérifier s'il y a des dommages, des tâches et des scellés cassés ou manquants. Tenir la base du plateau intérieur et retirer son couvercle.
5	Pour atteindre la bioprothèse, retirer le couvercle en plastique en tirant sur les deux languettes. Jeter le couvercle en plastique. HVT58  HVT54 
6	Fixer la poignée au système de support Tricentrix alors que la bioprothèse repose toujours sur le plateau. Pour cela, insérer la poignée dans le support et la tourner vers la droite jusqu'à sentir une résistance. HVT52  **Attention : ne pas saisir la bioprothèse avec les mains ou des instruments chirurgicaux.**

Étape	Procédure
	Attention : il faut éviter d'enchevêtrer l'étiquette avec le numéro de série dans la poignée lors de la fixation. **Attention : l'ensemble poignée-support est indispensable pour l'implantation et ne doit pas être retiré jusqu'à ce que la bioprothèse soit suturée sur l'anneau mitral.**
7	Une fois la poignée fixée, retirer l'ensemble du plateau (c.-à-d., le manchon de plastique, le clip, le système de support Tricentrix et la bioprothèse). Le manchon de plastique n'est pas solidement fixé au clip. Il se peut qu'il reste sur le plateau. Le déploiement n'en sera pas compromis. HVT53  Attraper le manchon de plastique ou le clip pour poursuivre la rotation jusqu'à ressentir une résistance, jusqu'à ce que le montant blanc du support soit en position déverrouillée. CP1089-23  Ou CP1089-6  CP1089-8 CP1089-9 Verrouillé Déverrouillé 

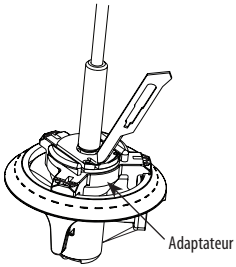
Étape	Procédure
8	Pousser la poignée jusqu'à ce que le montant blanc du support coulisse face aux valves et s'enclenche en position complètement déployée. Un déclic peut se faire entendre lorsque la position de déploiement est atteinte. CP1089-24 
9	**Attention : si la poignée n'est pas suffisamment poussée lors du déploiement du système de support Tricentrix, il se peut que le système échoue à réduire les risques de coincement de la suture.** Toujours vérifier que le déploiement est effectif. Il ne devrait plus exister aucun espace entre l'adaptateur bleu et le support gris. L'ensemble poignée-montant ne devrait plus pouvoir coulisser. Le montant blanc du support devrait dépasser à travers les valves, tandis que les trois commissures devraient être légèrement inclinées vers le centre de la bioprothèse. Le montant blanc du support déployé va plisser les valves de manière temporaire. Lorsque le support sera retiré après l'implantation, elles reprendront leur position normale. HVT56 
10	Après le déploiement, retirer le manchon (s'il est fixé) en tenant la poignée et en la tirant hors du clip. CP1089-25 

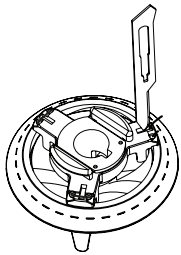
Étape	Procédure
11	Retirer le clip en le faisant glisser hors du support, vers le côté. CP1089-26  Jeter le manchon et le clip.
12	Une étiquette avec le numéro de série est fixée à l'anneau de suture de chaque bioprothèse par une suture. Ce numéro de série doit être comparé avec le numéro se trouvant sur l'emballage de la bioprothèse et sur la carte de données d'implantation de la bioprothèse. L'étiquette ne doit pas être détachée de la bioprothèse jusqu'à ce que l'implantation soit sûre. **Attention : si les numéros de série sont différents, la bioprothèse doit être renvoyée sans avoir été utilisée.** **Attention : il faut faire attention en coupant ou déchirant le tissu de l'anneau de suture lorsque l'étiquette du numéro de série est retirée.** **Attention : pour éviter d'endommager le tissu de l'anneau de suture, ne pas tirer sur la suture à travers l'anneau.**
13	**IL EST INUTILE DE RINCER** la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, avant l'implantation. **Attention : si la bioprothèse est rincée avant l'implantation, elle doit être ensuite conservée hydratée à l'aide d'une irrigation saline physiologique stérile sur les deux côtés du tissu de la valve pendant toute la durée de la procédure chirurgicale. Il est recommandé de la rincer toutes les une à deux minutes.** **Attention : éviter que le tissu de la valve entre en contact avec des serviettes, des linges ou d'autres sources de particules susceptibles de s'y transférer.**

10.4 Implantation du dispositif

Étape	Procédure
1	Le chirurgien doit être familier avec les recommandations concernant la mesure et le positionnement supra-annulaire (voir la section 10.2 Choix de la taille.) À cause de la complexité et de la variété du remplacement chirurgical de la valve cardiaque, le choix de la technique chirurgicale, correctement modifiée selon les **mises en garde** décrites précédemment, est à la discrétion du chirurgien individuel. En général, les étapes suivantes doivent être suivies : 1. Retirer par chirurgie les valves malades ou endommagées ainsi que toutes les structures associées au besoin. 2. Retirer par chirurgie le calcium de l'anneau afin d'assurer un bon positionnement de l'anneau de suture de la bioprothèse pour éviter d'endommager le tissu délicat de la valve. 3. Choisir la bonne taille. Mesurer l'anneau exclusivement à l'aide du calibreur mitral 1173B ou 1173R (figures 1a et 1b). 4. Bien positionner la prothèse. 5. Nouer les sutures une fois le support en place pour éviter qu'elles ne forment une boucle ou que la membrane ne se coince. 6. Examiner les valves de la bioprothèse pour repérer les déformations ou les fuites pouvant être survenues lors de l'étape précédente. **Attention : lors d'un choix d'une bioprothèse, il faut prendre en compte la taille, l'âge et l'état physique par rapport à la taille de la bioprothèse, afin de minimiser le risque d'hémodynamique sous-optimale. Toutefois, le choix final revient au médecin après l'évaluation des risques et des avantages pour le patient.** **Attention : il faut éliminer adéquatement les calcifications de l'anneau du patient avant l'implantation pour éviter que le tissu délicat de la valve bioprothétique ne s'endommage à leur contact. Insérer le calibreur dans l'anneau mitral. Le corps devrait toujours s'y adapter dans peine.** **Attention : n'utiliser que des calibreurs 1173B ou 1173R pour choisir la taille de la bioprothèse. L'emploi d'autres calibreurs peut conduire à un choix non adapté (voir 1.2 Description des accessoires). Comme pour les autres bioprothèses mitrales, l'implantation de la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, s'effectue généralement par la technique de suture discontinue matelassée. Cette technique est recommandée pour choisir la taille de l'anneau après le placement des sutures, ces dernières pouvant réduire la taille de la bioprothèse pouvant être implantée.**

Étape	Procédure
2	**Orientation adéquate de la bioprothèse :** **Attention : le fil métallique de la bioprothèse, modèle 11000M, est symétrique, et les trois supports des commissures (montants) sont équidistants. L'anneau de suture est cependant conçu en fonction d'une orientation donnée de la bioprothèse. La partie crénelée de l'anneau de suture, entre les deux protubérances en silicone, doit être placée face à la partie intercommissurale antérieure de l'anneau et enjamber la région de la voie d'évacuation du ventricule gauche.** Les marqueurs de suture en contraste de l'anneau de suture indiquent la bonne orientation et la distance type entre les commissures. Cette distance peut cependant varier d'un patient à l'autre. Sur le côté gauche, deux sutures noires rapprochées indiquent où placer le premier point et correspondent à la commissure antérieure. Le côté droit comporte une seule suture noire qui indique l'emplacement approximatif de la commissure postérieure. Lorsque ces guides d'orientation sont utilisés, le troisième montant se positionne naturellement vers le milieu de l'emplacement de la valve postérieure. **Attention : il convient de bien faire attention à ne pas placer un montant en face de la voie d'évacuation du ventricule gauche, car il pourrait compromettre le rendement hémodynamique sur le long terme.**
3	**Positionnement de la suture :** L'anneau de suture est encerclé par une ligne de guidage de suture en soie noire. Lors du positionnement des sutures à travers l'anneau de suture, la force de glissement est réduite lorsque les sutures sont placées directement à travers l'anneau de suture et dans la région, de la ligne de guidage à la partie externe de l'anneau de suture. Il faut maintenir une tension sur les sutures pendant que la bioprothèse est enfoncée dans l'anneau, afin de réduire les risques de formation de boucles susceptibles de coincer une valve. Une fois les montants d'endoprothèse complètement rétractés après la mise en place du système de support Tricentrix, il sera plus facile de guider les sutures vers la position adaptée derrière les montants et sur l'anneau de suture.

Étape	Procédure
	Retirer la poignée avant de nouer les sutures. La poignée et l'adaptateur bleu doivent être retirés en même temps. Maintenir la position de la bioprothèse dans l'anneau en plaçant délicatement le forceps ou les mains recouvertes de gants sur le support et en coupant le fil vert de l'adaptateur bleu. Retirer l'adaptateur bleu et la poignée en une seule opération. CP1089-27 
4	**Attention : éviter d'enrouler ou de coincer une suture autour des cages ouvertes, des montants libres ou des supports de commissures de la bioprothèse, sous peine de compromettre le bon fonctionnement de la valve. Pour réduire les risques d'enroulement des sutures, il est essentiel de laisser le support déployé en place jusqu'à ce que tous les nœuds soient faits.** Cependant, si le support gêne la vision du chirurgien, il faut nouer toutes les sutures proches des trois montants du cadre avant de couper les trois fils de fixation du support vert pour enlever le support. **Attention : si les fils de fixation du support déployé sont coupés avant que les sutures adjacentes ne soient nouées, le support n'empêchera plus l'enroulement des sutures autour des montants de la structure.** Il faut bien prendre soin d'éviter de nouer les sutures en haut des coins des tiges grises du support. Avant de nouer chaque suture, examiner les valves tout en tenant les deux brins sous tension. La déformation ou le déplacement des valves pendant cette étape indique que la suture est enroulée autour d'un montant. Il ne faut pas relâcher la tension sur les sutures avant ou après le retrait du support, sous peine de favoriser la formation de boucles et de coincer les sutures. Il est conseiller de passer un miroir chirurgical à travers les valves après le retrait du support afin d'examiner chaque montant ainsi que le positionnement des sutures. **Attention : lors de sutures séparées, il est important de les couper près des nœuds et de veiller à ce que le bout exposé n'entre pas en contact avec le tissu de la valve (réf. 8).**

Étape	Procédure
	Voici comment retirer le système de support Tricentrix en une seule opération à la fin des sutures : CP1089-14  1. À l'aide d'un scalpel ou de ciseaux placés uniquement dans le canal de coupe, couper chacune des trois (3) sutures vertes exposées. Ne jamais tenter de couper une suture sous un support partiellement détaché, car un fragment pourrait tomber dans le ventricule. Éviter de couper ou d'endommager l'endoprothèse ou le tissu de la valve en même temps que les sutures. 2. Après avoir coupé les trois (3) sutures du support, retirer le système de support Tricentrix de la bioprothèse en une seule opération, en même temps que vous nouez les sutures, en utilisant des gants ou des forceps protégés. 3. Après l'implantation, retirer et jeter la baguette.

10.5 Nettoyage et stérilisation des accessoires

Les accessoires de la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, sont emballés à part. La poignée du modèle 1126 est stérile et est destinée à un usage unique. Les poignées des modèles 1111, 1117 et 1173 et les calibreurs 1173B et 1173R ne sont pas stériles et doivent être nettoyés et stérilisés avant l'utilisation. Les poignées, les calibreurs, la base et le couvercle du plateau doivent être nettoyés et stérilisés à nouveau avant chaque utilisation. Consulter le mode d'emploi fourni avec les accessoires réutilisables pour connaitre les consignes de nettoyage et de stérilisation.

10.6 Retour de la bioprothèse

Edwards Lifesciences souhaite obtenir des échantillons cliniques recouverts de la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, à des fins d'analyse. Pour retourner des bioprothèses recouvertes, contacter votre représentant.

- Emballage non ouvert avec la barrière stérile intacte : si le sachet métallisé ou les plateaux n'ont pas été ouverts, retourner la bioprothèse dans son emballage d'origine.
- Emballage ouvert, mais avec la bioprothèse non implantée : si le plateau est ouvert, la bioprothèse n'est plus stérile. Si la bioprothèse n'est pas implantée, elle doit être placée dans un fixateur histologique adapté comme du méthanediol à 10 % ou du glutaraldéhyde à 2 %, puis retournée à l'entreprise. La réfrigération n'est pas nécessaire dans ces circonstances.
- Bioprothèse explantée : la bioprothèse explantée doit être placée dans un fixateur histologique adapté comme du méthanediol à 10 % ou du glutaraldéhyde à 2 %, puis retournée à l'entreprise. La réfrigération n'est pas nécessaire dans ces circonstances.

11. Sécurité dans l'environnement de résonance magnétique (RM)

Condition RM

Les tests non cliniques ont montré que la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, est conforme à la condition RM. Un patient possédant la bioprothèse, modèle 11000M, peut subir un balayage sans danger immédiatement après l'implantation, dans les conditions suivantes :

- Champ magnétique statique de 3 teslas ou moins
- Champ gradient spatial maximum de 720 gauss/cm
- Taux d'absorption spécifique maximal signalé par le système RM pour tout le corps de 3 W/kg pour un balayage de 15 minutes.

Pour les tests non cliniques, la bioprothèse mitrale péricardique d'Edwards, modèle 11000M, a produit une augmentation de température inférieure ou égale à 0,5 °C à un taux d'absorption spécifique (TAS) moyen maximum reporté par le système RM de 3 W/kg pendant un balayage RM de 15 minutes dans un système RM de 3 teslas (Excite, logiciel G3.0-052B, General Electric Healthcare).

Il est possible que la qualité de l'image RM soit compromise si la zone d'intérêt correspond à l'emplacement de la bioprothèse modèle 11000M ou en est relativement proche. Il est recommandé d'optimiser les paramètres d'imagerie RM.

12. Informations du patient

12.1 Carte d'identification de la recherche

Une carte d'identification de la recherche est remise à chaque sujet implanté avec la bioprothèse mitrale péricardique d'Edwards, modèle 11000M.

12.2 Documents d'information du patient

Il est possible d'obtenir des documents d'information du patient d'Edwards ou de l'un de ses spécialistes des ventes cliniques.

13. Références

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Se référer à la légende des symboles à la fin du document.

Tableau 3 : Taux observés d'évènements indésirables pour les RVM et les DRV (modèle 6900)

Tous les patients étudiés : N = 363 Suivi cumulatif : 1 100 patient-années

	Évènements précoces		Évènements tardifs[1]		Absence d'évènements (%) [IC de 95 %][2]		
Complication	n[3]	%	n	%/pt-an	1 an (n = 287)	5 ans (n = 141)	8 ans (n = 18)
Mortalité (tous)	34	9,4	50	4,7	85,5 [81,8, 89,2]	75,4 [70,3, 80,6]	65,4 [57,6, 73,2]
Évènements en lien avec la valve							
Mortalité (en lien avec la valve)	0	0	16	1,5	97,7 [96,0, 99,4]	95,3 [92,8, 97,8]	91,9 [87,5, 96,4]
Explantations	0	0	8	0,7	98,7 [98,0, 99,3]	96,7 [95,3, 98,0]	95,6 [93,9, 97,3]
Nouvelles opérations chirurgicales	2	0,6	12	1,1	97,1 [96,2, 98,1]	95,1 [93,6, 96,6]	93,0 [90,9, 95,1]
Hémorragie en lien avec l'anticoagulothérapie	2	0,6	9	0,8	97,1 [95,2, 99,0]	97,1 [95,2, 99,0]	94,1 [88,2, 100]
Endocardite	1	0,3	3	0,3	99,0 [97,9, 100]	98,7 [97,4, 98,9]	98,7 [97,4, 98,9]
Hémolyse	0	0,0	1	0,1	99,7 [99,0, 100]	99,7 [99,0, 100]	99,7 [99,0, 100]
Dysfonction non structurelle	0	0,0	3	0,3	100 [100, 100]	99,3 [98,0, 100]	98,3 [95,9, 100]
Fuite périvalvulaire (tous)	1	0,3	5	0,5	98,4 [97,0, 99,8]	98,4 [97,0, 99,8]	97,3 [94,9, 99,8]
Détérioration de la structure de la valve	0	0,0	5	0,5	100,0 [100, 100]	97,6 [95,2, 100]	92,8 [85,3, 100]
Thrombo-embolie	5	1,4	8	0,7	97,5 [95,8, 99,2]	96,1 [93,8, 98,5]	96,1 [93,8, 98,5]
Thrombose	0	0,0	0	0,0	100,0 [100, 100]	100,0 [100, 100]	100,0 [100, 100]

Remarques :

1. Les taux d'évènements tardifs sont calculés sous forme de taux linéarisés (%/pt-an) sur la base de 1 072,5 patient-années tardifs (> 30 jours après l'opération).
2. Les taux d'absence d'évènements ont été calculés avec la méthode Kaplan-Meier. La formule de Greenwood a été utilisée pour calculer les erreurs-types de ces estimations.
3. n = nombre d'évènements.

Tableau 4 : Taux observés d'évènements indésirables (modèle 6900P)

Tous les patients étudiés : N = 209 Suivi cumulatif : 873,18 total pt-an

	Évènements précoces		Évènements tardifs[1]		Absence d'évènements (%) [IC de 95 %][2]	
Complication	n[3]	%	n	%/pt-an	1 an	5 ans
Mortalité (tous)	3	1,4	45	5,3	93,2 [88,8, 95,9]	74,4 [66,9, 80,5]
Évènements en lien avec la valve						
Mortalité (en lien avec la valve)	1	0,5	12	1,4	98,5 [95,5, 99,5]	92,0 [86,2, 95,5]
Explantations	1	0,5	8	0,9	97,5 [94,0, 98,9]	96,5 [92,2, 98,5]
Nouvelles opérations chirurgicales	0	0,0	0	0,0	100,0 [100, 100]	100,0 [100, 100]
Saignements	5	2,4	13	1,5	96,1 [92,3, 98,0]	91,9 [86,5, 95,2]
Endocardite	1	0,5	3	0,4	99,5 [96,6, 99,9]	97,1 [92,1, 98,9]
Dysfonction non structurelle	0	0,0	1	0,1	99,5 [96,4, 99,9]	99,5 [96,4, 99,9]
Fuite périvalvulaire (tous)	1	0,5	2	0,2	99,5 [96,7, 99,9]	98,4 [95,2, 99,5]
Détérioration de la structure de la valve	0	0,0	2	0,2	100,0 [100, 100]	99,0 [93,2, 99,9]
Thrombo-embolie	4	1,9	12	1,4	97,0 [93,5, 98,7]	91,3 [85,8, 94,7]
Thrombose	0	0,0	0	0,0	100,0 [100, 100]	100,0 [100, 100]

Remarques :

1. Les taux d'évènements tardifs sont calculés sous forme de taux linéarisés (%/pt-an) sur la base de 856,24 patient-années tardifs (> 30 jours après l'opération).
2. Les taux d'absence d'évènements ont été calculés avec la méthode Kaplan-Meier. La formule de Greenwood a été utilisée pour calculer les erreurs-types de ces estimations.
3. n = nombre d'évènements.

Tableau 5 : Données démographiques préopératoires (modèle 6900)

Variable	Catégorie	Caractéristiques de l'étude (N = 363; 1 100 total pt-an)	
		n	% (n/N)[1]
Âge lors de l'implantation (N = 363)	Moyenne ± écart-type	66,1 ± 10,7	
Sexe	Fém./masc.	212/151	58,4%/41,6%
Diagnostique/étiologie	Aucune	30	8,3%
	Sténose	91	25,1%
	Régurgitation	184	50,7%
	Maladies mixtes	58	16,0%

Remarque :

1. n = nombre de patients pour chaque catégorie; N = total de patients de l'étude.

Tableau 6 : Données démographiques préopératoires (modèle 6900P)

Variable	Catégorie	Caractéristiques de l'étude (N = 209; 873,18 total pt-an)	
		n	% (n/N)[1]
Âge lors de l'implantation (N = 209)	Moyenne ± écart-type	71,4 ± 9,4	
Sexe	Fém./masc.	138/71	66,0%/34,0%
Diagnostique/étiologie	Maladies mixtes	48	23,0%
	Régurgitation	121	57,9%
	Sténose	32	15,3%
	Dysfonction de la valve	8	3,8%

Remarque :

1. n = nombre de patients pour chaque catégorie; N = total de patients de l'étude.

Tableau 7 : Données démographiques des patients en période opératoire (modèle 6900)

		Caractéristiques de l'étude (N = 363; 1 100 total pt-an)	
Variable	Catégorie	n	% (n/N)[1]
Étiologie[2]	Rhumatisme cardiaque	135	37,2%
	Calcification	82	22,6%
	Dégénération	50	13,8%
	Endocardite	39	10,7%
	Bioprothèse défectueuse	15	4,1%
	Cardiopathie ischémique	14	3,9%
	Anomalies congénitales	8	2,2%
	Autre	44	12,1%
Procédures concomitantes[2]	Aucune	200	55,1%
	PA[3]	78	21,5%
	Réparation tricuspidienne	61	16,8%
	Pompe à ballonnet intra aortique	17	4,7%
	Stimulateur cardiaque[4]	6	1,7%
	Réparation/remplacement aortique	5	1,4%
	Réparation d'un anévrisme	4	1,1%
	Autre	31	8,5%
Affections préexistantes[2]	Aucune	122	33,6%
	C[5] / PA	72	19,8%
	Hypertension	61	16,8%
	Fibrillation auriculaire	53	14,6%
	IM antérieur[6]	45	12,4%
	Maladie cérébrovasculaire	36	9,9%
	Autre	234	64,5%
Taille de la valve (mm)	25	22	6,1%
	27	110	30,3%
	29	137	37,7%
	31	81	22,3%
	33	13	3,6%

Remarques :

1. n = nombre de patients pour chaque catégorie; N = total des patients de l'étude
2. Possibilité de plus d'un par patient
3. PA = Pontage aortocoronarien
4. Permanent ou temporaire
5. C = Coronaropathie
6. IM = Infarctus du myocarde

Tableau 8 : Données démographiques des patients en période opératoire (modèle 6900P)

		Caractéristiques de l'étude (N = 209; 873,18 total pt-an)	
Variable	Catégorie	n	% (n/N)[1]
Étiologie[2]	Calcification	38	18,2%
	Congénital	1	0,5%
	Dégénératif	105	50,2%
	Endocardite récente	10	4,8%
	Ischémique	12	5,7%
	Rhumatismal	64	30,6%
	Autre	36	17,2%
Procédures concomitantes[2]	Aucune	91	43,5%
	Réparation valve/anneau aortique	3	1,4%
	PA[3]	58	27,8%
	Stimulateur cardiaque permanent	1	0,5%
	Réparation de la valve/anneau tricuspide	21	10,0%
	Autre	78	37,3%
Affections préexistantes[2]	Aucune	17	8,1%
	Arythmie	95	45,5%
	C[6]	85	40,7%
	Myocardiopathie	13	6,2%
	Insuffisance cardiaque congestive	66	31,6%
	Endocardite	14	6,7%
	Infarctus du myocarde	21	10,0%
	Maladie vasculaire périphérique	9	4,3%
	Hypertension artérielle pulmonaire	66	31,6%
	Fièvre rhumatismale	16	7,7%
	Hypertension généralisée	49	23,4%
	AIT[4]/AVC[5]	24	11,5%
	Autre	35	16,7%
Taille de la valve (mm)	25	28	13,4%
	27	37	17,7%
	29	84	40,2%
	31	43	20,6%
	33	17	8,1%

Remarques :

1. n = nombre de patients pour chaque catégorie; N = total des patients de l'étude
2. Possibilité de plus d'un par patient
3. PA = Pontage aortocoronarien
4. AIT = accident ischémique transitoire
5. AVC = accident vasculaire cérébral
6. C = Coronaropathie

Tableau 9 : Résultats en matière d'efficacité, classification fonctionnelle NYHA (modèle 6900)

Classification fonctionnelle de la NYHA	Évaluation préopératoire		Évaluations postopératoires			
			1 à 2 ans		5 ans	
	n/N[1]	%	n/N	%	n/N	%
I	11/363	3,0	120/268	44,8	40/129	31,0
II	73/363	20,1	90/268	33,6	25/129	19,4
III	192/363	52,9	15/268	5,6	1/129	0,8
IV	84/363	23,1	0/268	0,0	0/129	0,0
Non disponible	3/363	0,8	43/268	16,0	63/129	48,8

Remarque :

1. n = nombre de patients pour chaque catégorie; N = total de patients de l'étude.

Tableau 10 : Résultats en matière d'efficacité, classification fonctionnelle NYHA (modèle 6900P)

Classification fonctionnelle de la NYHA	Évaluation préopératoire		Évaluations postopératoires			
			1 an		5 ans	
	n/N[1]	%	n/N	%	n/N	%
I	6/209	2,9	86/187	46,0	30/96	31,3
II	27/209	12,9	68/187	36,4	33/96	34,4
III	121/209	57,9	8/187	4,3	6/96	6,3
IV	55/209	26,3	1/187	0,5	0/96	0,0
Non disponible	0/209	0,0	24/187	12,8	27/96	28,1

Remarque :

1. n = nombre de patients pour chaque catégorie; N = total de patients de l'étude.

Tableau 11 : Résultats en matière d'efficacité, résultats hémodynamiques[1] (modèle 6900)

Paramètre hémodynamique	Résultats par taille de valve				
	25 mm	27 mm	29 mm	31 mm	33 mm
Sortie/précoce post-implantation (n = 130, 109 RVM[2] et 21 DRV[3])					
Gradient moyen[4]	n = 3	n = 23	n = 36	n = 23	n = 3
• moyenne ± écart-type	5,7 ± 1,2	4,2 ± 1,7	4,2 ± 1,7	3,6 ± 1,0	7,5 ± 5,8
• min., max.	5, 7	2, 9	1, 8	2, 5	3, 14
SEO[5]	n = 1	n = 17	n = 22	n = 25	n = 5
• moyenne ± écart-type	1,5	2,9 ± 0,9	3,1 ± 0,9	2,5 ± 0,7	3,0 ± 1,2
• min., max.	1,5, 1,5	1,3, 4,1	1,4, 4,2	1,5, 3,8	1,6, 4,9
Régurgitation[6]	n = 3	n = 28	n = 51	n = 40	n = 8
0	3/3 (100%)	22/28 (79%)	36/51 (71%)	30/40 (75%)	4/8 (50%)
1+	0/3 (0%)	5/28 (18%)	13/51 (25%)	7/40 (18%)	4/8 (50%)
2+	0/3 (0%)	0/28 (0%)	1/51 (2%)	3/40 (7%)	0/8 (0%)
3+	0/3 (0%)	0/28 (0%)	1/51 (2%)	0/40 (0%)	0/8 (0%)
4+	0/3 (0%)	0/28 (0%)	0/51 (0%)	0/40 (0%)	0/8 (0%)
Non disponible	0/3 (0%)	1/28 (3%)	0/51 (0%)	0/40 (0%)	0/8 (0%)
Intervalle de 3 à 6 mois post-implantation (n = 49, 42 RVM[2] et 7 DRV[3])					
Gradient moyen[4]	n = 5	n = 19	n = 15	n = 5	n = 2
• moyenne ± écart-type	6,4 ± 1,7	5,3 ± 5	3,4 ± 1,2	4 ± 1,9	4 ± 0
• min., max.	5, 9	2, 25	2, 6	2, 7	4, 4
SEO[5]	n = 5	n = 18	n = 13	n = 5	n = 2
• moyenne ± écart-type	2,9 ± 0,8	2,6 ± 0,7	2,8 ± 0,6	2,9 ± 0,3	2,6 ± 1
• min., max.	1,8, 3,6	1,5, 5	2, 3,8	2,4, 3,3	2, 3,3
Régurgitation[6]	n = 5	n = 21	n = 15	n = 6	n = 2
0	3/5 (60%)	17/21 (81%)	6/15 (40%)	4/6 (67%)	1/2 (50%)
1+	0/5 (0%)	4/21 (19%)	8/15 (53%)	2/6 (33%)	0/2 (0%)
2+	1/5 (20%)	0/21 (0%)	1/15 (7%)	0/6 (0%)	1/2 (50%)
3+	0/5 (0%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)
4+	1/5 (20%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)
Non disponible	0/5 (0%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)

Suite sur la page suivante.

Tableau 11 : Résultats en matière d'efficacité, résultats hémodynamiques[1] (modèle 6900), suite

Paramètre hémodynamique	Résultats par taille de valve				
	25 mm	27 mm	29 mm	31 mm	33 mm
Intervalle de 1 à 2 ans après implantation (n = 131, 114 RVM[2] et 17 DRV[3])					
Gradient moyen[4]	n = 3	n = 40	n = 47	n = 27	n = 4
• moyenne ± écart-type	5,2 ± 0,7	4,1 ± 1,6	3,5 ± 1,8	3,1 ± 1,4	2,1 ± 0,5
• min., max.	4,7, 6	1, 7	1, 10	1, 7	1,5, 2,7
SEO[5]	n = 2	n = 35	n = 46	n = 29	n = 5
• moyenne ± écart-type	1,8 ± 0,4	2,3 ± 0,6	2,6 ± 0,5	2,6 ± 0,7	2,5 ± 0,5
• min., max.	1,5, 2,0	1,2, 3,5	1,1, 3,7	1,1, 3,7	2,1, 3,2
Régurgitation[6]	n = 4	n = 42	n = 51	n = 29	n = 5
0	2/4 (50%)	31/42 (74%)	36/51 (71%)	17/29 (59%)	3/5 (60%)
1+	1/4 (25%)	9/42 (21%)	11/51 (21%)	8/29 (27%)	1/5 (20%)
2+	1/4 (25%)	2/42 (5%)	4/51 (8%)	2/29 (7%)	1/5 (20%)
3+	0/4 (0%)	0/42 (0%)	0/51 (0%)	2/29 (7%)	0/5 (0%)
4+	0/4 (0%)	0/42 (0%)	0/51 (0%)	0/29 (0%)	0/5 (0%)
Non disponible	0/4 (0%)	0/42 (0%)	0/51 (0%)	0/29 (0%)	0/5 (0%)
Intervalle de 5 ans après implantation (n = 11, 9 RVM[2] et 2 DRV[3])					
Gradient moyen[4]	n = 0	n = 6	n = 5	n = 0	n = 0
• moyenne ± écart-type	S.O.	8,8 ± 8,1	5,1 ± 2,3	S.O.	S.O.
• min., max.	S.O.	4, 25	3, 8	S.O.	S.O.
SEO[5]	n = 0	n = 2	n = 4	n = 0	n = 0
• moyenne ± écart-type	S.O.	2,0 ± 1,5	2,9 ± 0,6	S.O.	S.O.
• min., max.	S.O.	1,0, 3,1	2,1, 3,5	S.O.	S.O.
Régurgitation[6]	n = 0	n = 6	n = 5	n = 0	n = 0
0	0/0 (0%)	4/6 (66%)	2/5 (40%)	0/0 (0%)	0/0 (0%)
1+	0/0 (0%)	1/6 (17%)	3/5 (60%)	0/0 (0%)	0/0 (0%)
2+	0/0 (0%)	1/6 (17%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
3+	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
4+	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
Non disponible	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)

Remarques :

1. Les évaluations hémodynamiques ont été effectuées par échocardiographie transthoracique et, dans certains cas, par échocardiographie transoesophagienne.
2. RVM = remplacement de la valve mitrale
3. DRV = double remplacement de la valve
4. Gradient moyen en mm Hg
5. SEO : surface effective d'orifice, cm^2
6. Régurgitation = aucune, 0; bénigne, 1+; modérée, 2+; modérée à grave, 3+; grave, 4+

Tableau 12 : Résultats en matière d'efficacité, résultats hémodynamiques (modèle 6900P)[1]

Paramètre hémodynamique	Résultats par taille de valve				
	25 mm	27 mm	29 mm	31 mm	33 mm
Sortie/précoce post-implantation					
Gradient moyen[2]	n = 24	n = 35	n = 83	n = 42	n = 16
• moyenne ± écart-type	6,4 ± 1,87	4,4 ± 1,52	3,4 ± 1,47	3,3 ± 1,20	4,0 ± 1,38
• min., max.	3, 10	1,96, 8	1,4, 9	1, 7	1,5, 6,91
SEO[3]	n = 8	n = 27	n = 77	n = 41	n = 16
• moyenne ± écart-type	2,7 ± 0,87	2,8 ± 0,58	2,9 ± 0,93	2,5 ± 0,67	2,4 ± 0,52
• min., max.	1,46, 4,4	1,5, 3,9	1,58, 6	1,32, 4,2	1,55, 3,31
Régurgitation[4]	n = 27	n = 37	n = 83	n = 43	n = 17
Anodine/aucune	19/27 (70%)	29/37 (78%)	76/83 (92%)	39/43 (91%)	15/17 (88%)
1+ Bénigne	6/27 (22%)	7/37 (19%)	7/83 (8%)	4/43 (9%)	1/17 (6%)
2+ Modérée	1/27 (4%)	1/37 (3%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
3+ Modérée à grave	0/27 (0%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	1/17 (6%)
4+ Grave	0/27 (0%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
Non disponible	1/27 (4%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
Intervalle de 3 à 6 mois post-implantation					
Gradient moyen[2]	n = 0	n = 4	n = 3	n = 2	n = 0
• moyenne ± écart-type	0 ± 0	4,4 ± 2,25	2,3 ± 0,89	6,6 ± 2,05	0 ± 0
• min., max.	0, 0	2,5, 7,5	1,3, 3	5,1, 8	0, 0
SEO[3]	n = 0	n = 3	n = 3	n = 1	n = 1
• moyenne ± écart-type	0 ± 0	2,4 ± 0,74	3,2 ± 0,88	2,5 ± 0,00	1,2 ± 0,00
• min., max.	0, 0	1,6, 3	2,3, 4,05	2,47, 2,47	1,22, 1,22
Régurgitation[4]	n = 0	n = 5	n = 3	n = 2	n = 2
Anodine/aucune	0	3/5 (60%)	2/3 (67%)	2/2 (100%)	2/2 (100%)
1+ Bénigne	0	1/5 (20%)	1/3 (33%)	0/2 (0%)	0/2 (0%)
2+ Modérée	0	1/5 (20%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
3+ Modérée à grave	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
4+ Grave	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
Non disponible	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)

Suite sur la page suivante.

Tableau 12 : Résultats en matière d'efficacité, résultats hémodynamiques (modèle 6900P)[1], suite

Paramètre hémodynamique	Résultats par taille de valve				
	25 mm	27 mm	29 mm	31 mm	33 mm
Intervalle de 1 an après implantation					
Gradient moyen[2]	n = 16	n = 27	n = 63	n = 34	n = 15
• moyenne ± écart-type	5,9 ± 2,36	4,0 ± 1,45	3,0 ± 1,61	3,3 ± 1,26	3,4 ± 1,25
• min., max.	3, 12	2, 7	1, 12	1,5, 7	1,9, 6,3
SEO[3]	n = 3	n = 21	n = 59	n = 32	n = 15
• moyenne ± écart-type	2,3 ± 0,16	2,4 ± 0,76	2,6 ± 0,74	2,5 ± 0,67	2,3 ± 0,83
• min., max.	2,09, 2,4	1,27, 4,76	1,5, 5,7	1,5, 4	1,2, 3,8
Régurgitation[4]	n = 20	n = 28	n = 65	n = 34	n = 16
Anodine/aucune	17/20 (85%)	24/28 (86%)	53/65 (82%)	29/34 (85%)	13/16 (81%)
1+ Bénigne	3/20 (15%)	3/28 (11%)	6/65 (9%)	3/34 (9%)	3/16 (19%)
2+ Modérée	0/20 (0%)	0/28 (0%)	3/65 (5%)	2/34 (6%)	0/16 (0%)
3+ Modérée à grave	0/20 (0%)	0/28 (0%)	1/65 (2%)	0/34 (0%)	0/16 (0%)
4+ Grave	0/20 (0%)	0/28 (0%)	0/65 (0%)	0/34 (0%)	0/16 (0%)
Non disponible	0/20 (0%)	1/28 (4%)	2/65 (3%)	0/34 (0%)	0/16 (0%)

Remarques :

1. Les évaluations hémodynamiques ont été effectuées par échocardiographie transthoracique et, dans certains cas, par échocardiographie transoesophagienne.
2. Gradient moyen en mm Hg
3. SEO: surface effective d'orifice, cm^2
4. Régurgitation = anodine/aucune 0; bénigne, 1+; modérée, 2+; modérée à grave, 3+; grave, 4+

Polski

Osierdziowa bioproteza mitralna Edwards model 11000M

Instrukcja użytkowania

PRZESTROGA: Urządzenie badawcze. Prawo federalne (Stanów Zjednoczonych Ameryki) ogranicza użytkowanie tego urządzenia do celów badawczych.

PRZESTROGA: Urządzenie badawcze. Wyłącznie do badań klinicznych.

Przestroga: Urządzenie badawcze. Przeznaczone wyłącznie do celów badawczych. Do stosowania wyłącznie przez wykwalifikowanych badaczy (lekarzy).

1. Opis urządzenia i akcesoriów

1.1 Opis urządzenia

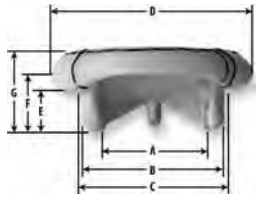
Osierdziowa bioproteza mitralna Edwards model 11000M jest trójpłatkową bioprotezą wykonaną z odpowiednio przygotowanego wołowego osierdzia, umocowaną na elastycznej ramie. Jest dostępna w rozmiarach 25, 27, 29, 31 i 33 mm (Tabela 1). Bioproteza jest przechowywana w opakowaniu niewodnym i nie wymaga przemywania przed wszczepieniem.

Prowadnica druciana jest wykonana ze stopu kobaltowo-chromowego i jest pokryta tkaniną poliestrową. Stop kobaltowo-chromowy/warstwa laminatu poliestrowego otacza podstawę ramy prowadnicy drucianej.

Silikonowy pierścień do wszywania o strukturze waflowej, pokryty porowatą tkaniną politetrafluoroetylenową (PTFE), jest przymocowany do ramy prowadnicy drucianej. Pierścień do wszywania jest obrębiony wzdłuż przedniej części. Szwy znacznikowe z czarnego jedwabiu na przedniej części ułatwiają ułożenie bioprotezy i pomagają zapobiec zablokowaniu drogi odpływu z lewej komory przez rozpórkę.

Linia prowadząca szew z czarnego jedwabiu otacza pierścień do wszywania. Umieszczanie szwów przechodzących przez pierścień do wszywania i w regionie od linii prowadzącej szew do zewnętrznej części pierścienia do wszywania ułatwia penetrację igły i zapewnia zmienną zgodność. W strukturze waflowej komórki są szersze wzdłuż części tylnej, gdzie w naturalnym pierścieniu mitralnym częstsze są zwapnienia i nieregularności (poz. 6).

Tabela 1: Wymiary nominalne



HVT63

Rozmiar	25 mm	27 mm	29 mm	31 mm	33 mm
A. Średnica stentu (prowadnica druciana, mm)	25	27	29	31	31
B. Średnica pierścienia tkanki (mm)	28	29,5	31,5	33,5	33,5
C. Zewnętrzna średnica wspornika stentu (końcówka, mm)	29	31	34	35	35
D. Zewnętrzna średnica pierścienia do wszywania (mm)	36	38	40	42	44
E. Efektywny profil – część przednia (mm)	7	7,5	8	8,5	8,5
E. Efektywny profil – część tylna (mm)	10	10,5	11	11,5	11,5
G. Całkowita wysokość profilu (mm)	15	16	17	18	18
Powierzchnia geometryczna otworu (mm^2)	424	499	580	653	653

1.2 Opis akcesoriów

Do bioprotezy 11000M dostępne są następujące akcesoria:

- system uchwytu Tricentrix
- kalibrator replikujący 1173R
- kalibrator cylindra 1173B
- taca do wyjaławiania dostarczana z modelem SET1173
- modele rękojeści 1111, 1117, 1173 i 1126 (do jednorazowego użytku)

Wszelkie akcesoria są dostarczane jako niejałowe, z wyjątkiem systemu uchwytu Tricentrix, dostarczanego w postaci jałowej i dołączonego do jałowej bioprotezy, oraz rękojeści 1126, dostarczanej w postaci jałowej i przeznaczonej do jednokrotnego użycia.

Kalibratory i taca

Z bioprotezą 11000M można stosować wyłącznie modele kalibratorów 1173B (Rysunek 1a) lub 1173R (Rysunek 1b).

Przestroga: Do określania rozmiaru bioprotezy 11000M nie należy używać kalibratorów zastawkowych innych producentów ani kalibratorów przeznaczonych do innych protez zastawkowych firmy Edwards Lifesciences.

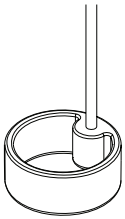
Do ustalenia odpowiedniego rozmiaru bioprotezy 11000M należy używać wyłącznie kalibratorów model 1173B i 1173R. Kalibratory 1173B i 1173R umożliwiają bezpośrednią obserwację dopasowania w pierścieniu włóknistym. Są dostarczane dla każdego z dostępnych rozmiarów bioprotezy 11000M. Cylindry kalibratorów model 1173B i 1173R wskazują zewnętrzną średnicę stentu przy

podstawie. Krawędź kalibratorów replikujących 1173R powiela kształt pierścienia do wszywania bioprotezy z jego przednią, obrębioną częścią oraz czarnymi znacznikami. Ma to na celu lepsze ustalenie wyników stosowania specyficznych technik wszywania lub technik zabezpieczenia aparatu podzastawkowego.

Kalibratory 1173B i 1173R są oznaczone rozmiarem bioprotezy. Kompletny zestaw kalibratorów jest umieszczony na tacy model SET1173, którą można ponownie wykorzystywać i sterylizować.

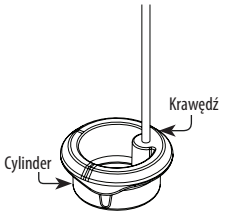
Rysunek 1a – 1173B kalibrator cylindra

CP1089-16



Rysunek 1b – 1173R kalibrator replikujący

CP1089-15

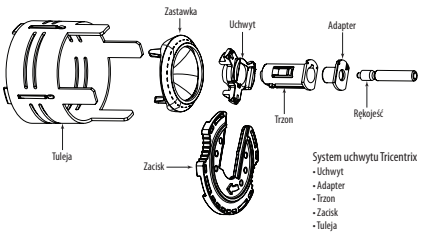


System uchwytu Tricentrix i rękojeści

Zespół uchwyt/rękojeść składa się z dwóch części: systemu uchwytu Tricentrix (Rysunek 2), który jest mocowany do bioprotezy 11000M, i rękojeści (1111, 1117, 1173 lub 1126), która jest dołączana do systemu uchwytu Tricentrix podczas zabiegu.

Rysunek 2 – System uchwytu Tricentrix

CP1089-28



HVT55

Poniższe rękojeści (Tabela 2) mogą być stosowane z bioprotezą 11000M:

Tabela 2. Rękojeści akcesoriów

Model	Materiał korpusu	Całkowita długość		Do wielokrotnego użytku
		cale	cm	
1111	Stal nierdzewna	7,0	17,8	Tak
1117	Nitinol	9,1	23,2	Tak
1126	Stal nierdzewna	11,5	29,2	Nie
1173	Nitinol	11,3	28,6	Tak

Rękojeści o trzonie nitinolowym są elastyczniejsze od uchwytów ze stali nierdzewnej. Po każdym cyklu wyjaławiania powracają do oryginalnego, prostego kształtu, co pozwala na łatwiejsze przymocowanie uchwytu.

2. Wskazania do stosowania

Osierdziowa bioproteza mitralna Edwards model 11000M jest przeznaczona dla pacjentów wymagających wymiany naturalnej lub protetycznej zastawki mitralnej.

3. Przeciwwskazania

Nie należy stosować produktu, jeżeli chirurg sądzi, że jego użycie jest sprzeczne z dobrem pacjenta. To on powinien podjąć decyzję dotyczącą zastosowania tej bioprotezy lub zrezygnowania z jej użycia, ponieważ może ocenić różne czynniki ryzyka związane z jej wszczepieniem, w tym również budowę anatomiczną pacjenta oraz zmiany patologiczne widoczne podczas operacji.

4. Ostrzeżenia

WYŁĄCZNIE DO JEDNORAZOWEGO UŻYTKU. Opisywane urządzenie jest zaprojektowane i rozprowadzane wyłącznie z zamiarem jednorazowego użytku i takie jest jego przeznaczenie. Urządzenia nie wolno sterylizować ani stosować ponownie. Nie istnieją żadne dane potwierdzające jałowość, niepirogenność i sprawność produktu po ponownej sterylizacji. Wystawienie bioprotezy lub pojemnika na działanie promieniowania, pary, tlenku etylenu lub innych chemicznych środków sterylizujących spowoduje, że bioproteza będzie niezdatna do użytku.

NIE WOLNO ZAMRAŻAĆ BIOPROTEZY ANI PODDAWAĆ DZIAŁANIU SKRAJNIE WYSOKIEJ TEMPERATURY. Narażenie bioprotezy na skrajne temperatury uczyni urządzenie niezdatnym do użycia.

Bioprotezy NIE NALEŻY UŻYWAĆ:

- **jeśli torebka foliowa, zapieczętowane tace lub pokrywy są otwarte, uszkodzone lub zabrudzone**
- **jeśli minął termin ważności lub**
- **jeśli została upuszczona, zniszczona lub postępowano z nią w niewłaściwy sposób. Jeśli podczas wszczepiania bioproteza ulegnie zniszczeniu, nie należy podejmować próby jej naprawy.**

NIE NALEŻY NARAŻAĆ bioprotezy na działanie jakichkolwiek roztworów, środków chemicznych, antybiotyków itp., z wyjątkiem jałowego roztworu soli fizjologicznej. Może nastąpić nienaprawialne uszkodzenie tkanki płatków, które może nie być widoczne gołym okiem.

NIE WOLNO CHWYTAĆ tkanki płatków bioprotezy narzędziami ani w żaden sposób uszkadzać bioprotezy. Nawet najmniejsza perforacja tkanki płatków może z czasem ulec powiększeniu, powodując znaczne upośledzenie czynności zastawki.

NIE NALEŻY STOSOWAĆ ZBYT DUŻEGO ROZMIARU. Stosowanie zbyt dużego rozmiaru może spowodować uszkodzenie bioprotezy lub miejscowe naprężenia mechaniczne, których efektem może być uszkodzenie serca, zniszczenie tkanki płatków, zniekształcenie stentu i przepływ fali zwrotnej przez zastawkę.

NIE PRZEPROWADZAĆ PRZEZ BIOPROTEZĘ CEWNIKÓW, wprowadzanych do żył elektrod stymulujących ani żadnych narzędzi chirurgicznych, z wyjątkiem lusterka chirurgicznego używanego do sprawdzania umieszczenia rozpórek i szwów. Pozostałe narzędzia chirurgiczne mogą spowodować uszkodzenie tkanki płatków.

Podobnie jak w przypadku każdego implantowanego przyrządu medycznego, istnieje ryzyko odpowiedzi immunologicznej u pacjenta. Do składników modelu 11000M należy stop metalu, który zawiera kobalt, chrom, nikiel, molibden, mangan, węgiel, beryl oraz żelazo. Należy zachować ostrożność u pacjentów z nadwrażliwościami na te materiały. Urządzenie zostało wytworzone bez lateksu, ale mogło być produkowane w środowisku zawierającym lateks.

5. Zdarzenia niepożądane

5.1 Zaobserwowane zdarzenia niepożądane

Podobnie jak w przypadku wszystkich sztucznych zastawek serca, stosowanie zastawek tkankowych może wiązać się z poważnymi działaniami niepożądanymi, niekiedy prowadzącymi do zgonu. Ponadto po upływie różnych okresów czasu (godzin lub dni) mogą występować zdarzenia niepożądane wynikające z indywidualnej reakcji pacjenta na wszczepione urządzenie lub fizycznych i chemicznych zmian jego komponentów, zwłaszcza pochodzenia biologicznego; mogą one powodować konieczność ponownej operacji i wymiany protezy.

Osierdziowa bioproteza mitralna Edwards model 11000M jest podobna w konstrukcji do bioprotez osierdziowych Carpentier-Edwards PERIMOUNT Magna Mitral Ease model 7300TFX.

Przeprowadzono trzy (3) wieloośrodkowe, nierandomizowane, prospektywne badania kliniczne, poza terenem Stanów Zjednoczonych, u pacjentów z zaimplantowaną bioprotezą osierdziową zastawki mitralnej model 6900. Trzystu jeden (301) pacjentów poddanych zostało izolowanej wymianie zastawki mitralnej (MVR), a 62 wymianie dwóch zastawek (DVR), przy czym zastawka aortalna była wymieniana na bioprotezę osierdziową PERIMOUNT firmy Carpentier-Edwards model aortalny.

W pierwszym badaniu bioprotezy wszczepiano w latach od 1984 do 1986, w drugim badaniu bioprotezy wszczepiano w latach od 1989 do 1994, w trzecim badaniu bioprotezy wszczepiano w latach od 1996 do 1997. Stan pacjentów oceniano przedoperacyjnie, śródoperacyjnie, przy wypisywaniu ze szpitala, po 1 roku i następnie corocznie. Przez cały okres pooperacyjny notowano występowanie zdarzeń niepożądanych.

Tabela 3 przedstawia częstość obserwowanych zdarzeń wczesnych dla modelu 6900 (≤ 30 dni w przypadku zdarzeń niepożądanych związanych z zastawką), liniowo przedstawia częstość zdarzeń późnych (> 30 dni po zabiegu) oraz aktuarialną częstość zdarzeń niepożądanych po 1 roku, 5 latach i 8 latach po zabiegu. Częstości występowania zdarzeń niepożądanych pochodzą od 363 pacjentów w dziewięciu ośrodkach. Zbiorczy czas obserwacji wyniósł 1100 pacjentolat ze średnim czasem obserwacji wynoszącym 3,0 roku (SD = 2,4 roku, zakres = 0 do 8,2 lat). Przedoperacyjne i pochodzące z okresu operacji dane demograficzne pacjentów zostały przedstawione w tabelach 5 i 7. Wyniki dotyczące skuteczności operacji zostały przedstawione w tabelach 9 i 11.

Przeprowadzono jedno (1) wieloośrodkowe, nierandomizowane, prospektywne, międzynarodowe badanie kliniczne u pacjentów z zaimplantowaną bioprotezą osierdziową zastawki mitralnej Carpentier-Edwards PERIMOUNT Plus model 6900P. U stu siedemdziesięciu pięciu (175) pacjentów przeprowadzono zabieg izolowanej wymiany zastawki mitralnej (MVR), a u 34 pacjentów zabieg wymiany dwóch zastawek (DVR) z wymianą zastawki aortalnej na bioprotezę osierdziową zastawki aortalnej Carpentier-Edwards PERIMOUNT. W tym badaniu implantacje przeprowadzano w latach 1999-2007. Stan pacjentów oceniano przedoperacyjnie, śródoperacyjnie/przy wypisywaniu ze szpitala, po 1 roku, a następnie corocznie. Przez cały okres pooperacyjny notowano występowanie zdarzeń niepożądanych. Tabela 4 przedstawia częstość obserwowanych zdarzeń wczesnych dla modelu 6900P (≤ 30 dni w przypadku zdarzeń niepożądanych związanych z zastawką), liniowo przedstawia częstość zdarzeń późnych (> 30 dni po zabiegu) oraz aktuarialną częstość zdarzeń niepożądanych po 1 roku i 5 latach po zabiegu. Częstości zdarzeń niepożądanych podano w oparciu o dane dotyczące dwustu dziewięciu (209) pacjentów z siedmiu ośrodków. Łączny okres obserwacji wyniósł 873,18 pacjentolat ze średnim okresem obserwacji 4,2 roku (SD = 2,3 roku, zakres = 0 do 8,2 lat). Przedoperacyjne i pochodzące z okresu operacji dane demograficzne pacjentów zostały przedstawione w tabelach 6 i 8. Wyniki dotyczące skuteczności operacji zostały przedstawione w tabelach 10 i 12.

5.2 Możliwe zdarzenia niepożądane

Zdarzenia niepożądane potencjalnie związane z zastosowaniem bioprotez zastawek serca to:

- Dławica piersiowa
- Skazy krwotoczne związane z leczeniem przeciwzakrzepowym (koagulopatia)
- Zaburzenia rytmu serca
- Zablokowanie ujścia wieńcowego
- Zapalenie wsierdzia
- Niewydolność serca
- Niedokrwistość hemolityczna
- Hemoliza
- Krwotok
- Miejscowe i/lub uogólnione zakażenie
- Zawał mięśnia sercowego
- Niedopasowanie protezy do pacjenta (PPM)
- Usidlenie płatka zastawki (wklinowanie)
- Niestrukturalna dysfunkcja protezy
- Wytworzenie łuszczki
- Przeciek okołozastawkowy
- Niedomykalność protezy
- Strukturalne uszkodzenie protezy
- Zakrzepica protezy
- Udar mózgu
- Zaburzenia zakrzepowo-zatorowe
- Przemijające niedokrwienie mózgu (TIA)

Wymienione powikłania mogą prowadzić do:

- Powtórnego zabiegu operacyjnego
- Usunięcia zastawki
- Trwałej niepełnosprawności
- Zgonu

Inne zdarzenia niepożądane, związane z zastosowaniem osierdziowej bioprotezy zastawki mitralnej Carpentier-Edwards PERIMOUNT model 6900, zebrane w literaturze oraz pochodzące z doniesień otrzymanych z systemu obsługi reklamacji firmy Edwards Lifesciences obejmują: stenozę, niedomykalność niewydolnej zastawki, perforację komory wspornikami stentów, niesprawność zastawki z powodu odkształcenia implantu, pęknięcie ramy prowadnicy drucianej.

6. Badania kliniczne

Punktami końcowymi bezpieczeństwa uchwyconymi w badaniach prospektywnych były zdarzenia niepożądane; stosowano analizy krwi w celu potwierdzenia nieobecności lub obecności określonych zdarzeń niepożądanych. Wyniki bezpieczeństwa dla modelu 6900 zaprezentowano w tabeli 3, a dla modelu 6900P w tabeli 4. Przedoperacyjne dane demograficzne pacjentów dla modelu 6900 zostały przedstawione w tabeli 5, a dla modelu 6900P w tabeli 6. Operacyjne dane demograficzne pacjentów, którym wszczepiono model 6900, podano w tabeli 7, a model 6900P – w tabeli 8. Punktami końcowymi skuteczności były klasyfikacja funkcjonalna Nowojorskiego Towarzystwa Kardiologicznego (NYHA) i badania echokardiograficzne. Podsumowanie wyników klasyfikacji zawarto w tabeli 9 dla modelu 6900 i tabeli 10 dla modelu 6900P. Wyniki badań echokardiograficznych podsumowano w tabeli 11 dla modelu 6900 i tabeli 12 dla modelu 6900P.

Brak danych klinicznych wskazujących na zwiększoną odporność osierdziowej bioprotezy mitralnej Edwards model 11000M na zwapnienie, w porównaniu do innych dostępnych na rynku bioprotez.

7. Indywidualizacja leczenia

Biorcy bioprotez zastawek serca powinni kontynuować leczenie przeciwzakrzepowe (z wyjątkiem przypadków, w których jest ono przeciwwskazane) w pierwszym okresie po wszczepieniu – w każdym przypadku według oceny lekarza. Długoterminowe leczenie przeciwzakrzepowe i/lub przeciwpłytkowe należy rozważyć u pacjentów z czynnikami ryzyka zaburzeń zakrzepowo-zatorowych.

Ostateczną decyzję w sprawie opieki nad konkretnym pacjentem powinien podjąć personel medyczny oraz pacjent, w świetle wszystkich okoliczności dotyczących tego pacjenta (poz. 7). Bioproteza jest zalecana do MVR u pacjentów w każdym wieku, którzy nie będą przyjmować warfaryny lub mają poważne przeciwwskazania medyczne do leczenia warfaryną. Preferencje pacjenta to racjonalne kryterium przy wyborze operacji wymiany zastawki mitralnej oraz wyborze protezy mitralnej. Mechaniczna proteza jest rozsądnym wyborem do MVR u pacjentów poniżej 65 roku życia, którzy nie mają przeciwwskazania do leczenia przeciwzakrzepowego. Bioprotеza jest rozsądnym wyborem do MVR u pacjentów poniżej 65 roku życia, którzy wybrali wymianę zastawki ze względów związanych ze stylem życia po szczegółowym omówieniu ryzyka leczenia przeciwzakrzepowego względem prawdopodobieństwa konieczności przeprowadzenia kolejnego zabiegu MVR (poz. 7).

7.1 Szczególne grupy pacjentów

Nie potwierdzono bezpieczeństwa ani skuteczności stosowania modelu bioprotez 11000M w następujących szczególnych populacjach, ponieważ nie przebadano ich w takich grupach:

- kobiety ciężarne;
- matki karmiące;
- pacjenci z nieprawidłowym metabolizmem wapnia (np. z przewlekłą niewydolnością nerek lub nadczynnością przytarczyc);
- pacjenci ze schorzeniami zwyrodnieniowymi aorty powodującymi powstawanie tętniaków (np. martwica torbielowata błony środkowej, zespół Marfana);
- dzieci, młodzież lub młode osoby dorosłe.

Przestroga: Na podstawie doniesień w piśmiennictwie na temat zastawek tkankowych (poz. 9, 10, 11, 12 i 13) wydaje się występować zwiększony odsetek zwapnienia listków u pacjentów w wieku poniżej 20 lat. Jeśli jest to możliwe, należy unikać powtarzanych dożylnych wstrzyknięć preparatów zawierających wapń w okresie pooperacyjnym, a u dzieci także nadmiernego spożycia mleka oraz nabiału. Wyniki badań prowadzonych na zwierzętach (poz. 14) wskazują, że wysoki poziom wapnia w organizmie może prowadzić do wczesnego powstawania zwapnień.

8. Informacja dla pacjenta

Po operacji zaleca się uważną i stałą obserwację lekarską (przynajmniej jedna wizyta rocznie), aby umożliwić rozpoznanie i właściwe leczenie powikłań związanych z bioprotezą, szczególnie wynikających z uszkodzenia materiału. Pacjentom z bioprotezą, którzy są w grupie podwyższonego ryzyka bakteriemii (np. mają być poddani zabiegom stomatologicznym), warto doradzić profilaktyczną terapię antybiotykową. Pacjentom należy doradzać, aby zawsze nosili przy sobie Kartę danych wszczepu oraz informowali pracowników służby zdrowia o posiadanym implancie przy zasięganiu porady lekarskiej.

9. Sposób dostarczania

9.1 Opakowanie

Osierdziowa bioproteza mitralna Edwards model 11000M jest dostarczana w postaci jałowej i niepirogennej w opakowaniu tacowym z podwójną ochroną. Opakowanie tacowe z podwójną ochroną mieści się w torebce foliowej, która znajduje się w kartonie.

Każda bioproteza umieszczona jest w kartonie ze wskaźnikiem temperatury widocznym przez okienko na panelu bocznym. Wskaźnik temperatury przeznaczony jest do umożliwienia identyfikacji produktów narażonych na przejściowe skrajne warunki temperaturowe. W chwili otrzymania bioprotezy należy niezwłocznie sprawdzić wskaźnik i zapoznać się z etykietą kartonu, aby potwierdzić stan „Do wykorzystania". Jeśli stan „Do wykorzystania" nie jest oczywisty, nie należy używać bioprotezy i skontaktować się z lokalnym dostawcą lub przedstawicielem firmy Edwards Lifesciences w celu dokonania ustaleń dotyczących potwierdzenia zwrotu i wymiany.

Ostrzeżenie: Dokładnie sprawdzić bioprotezę przed implantacją pod kątem dowodów ekspozycji na skrajne temperatury lub innych uszkodzeń.

9.2 Przechowywanie

Osierdziową bioprotezę mitralną Edwards model 11000M należy przechowywać w temperaturze 10°C do 25°C (50-77 °F), w torebce foliowej i kartonie, na półce.

10. Wskazówki dotyczące użycia

10.1 Szkolenia lekarzy

Techniki wszczepiania niniejszej bioprotezy są zbliżone do technik stosowanych przy wszczepianiu innych stentowych bioprotez zastawki mitralnej. Specjalne przeszkolenie lekarzy nie jest konieczne do wykonywania implantacji osierdziowej bioprotezy mitralnej Edwards model 11000M.

10.2 Kalibrowanie

Przestroga: Do określania rozmiaru bioprotezy 11000M nie należy używać kalibratorów zastawkowych innych producentów ani kalibratorów przeznaczonych do innych protez zastawkowych firmy Edwards Lifesciences.

Przestroga: Sprawdzić kalibratory i rękojeści pod kątem zużycia, takiego jak stępienie, pękanie lub spękanie włoskowate. W razie zauważenia jakichkolwiek objawów zużycia kalibrator lub rękojeść należy wymienić.

Ostrzeżenie: Fragmenty rękojeści i kalibratorów nie są radiologicznie nieprzezroczyste i nie można ich lokalizować za pomocą zewnętrznego urządzenia obrazującego.

Sprawdzić, czy akcesoria zostały wyjałowione zgodnie z zalecanymi instrukcjami dostarczonymi z akcesoriami wielorazowymi.

Czarne znaczniki na krawędzi odpowiadają czarnym szwom znacznikowym na pierścieniu do wszywania. Wyznaczają one przednią część pierścienia do wszywania bioprotezy, która powinna zostać umieszczona naprzeciw przedniej międzyspoidłowej części naturalnego pierścienia, aby objąć obszar odpływu z lewej komory. Wysokość i lokalizacja wsporników stentów jest oznaczona na kalibratorze 1173R, aby pomóc w optymalnym wyrównaniu i osadzeniu.

Kalibratory są dostarczane z wstępnie przymocowanymi rękojeściami, które wydłużają rękojeść dla lepszego dostępu w przypadku trudnych warunków, głębokiej klatki piersiowej lub dostępu minimalnie inwazyjnego. Przyłączenie do kalibratora rękojeści tylnej zapewnia nieograniczany wgląd przez cylinder do komory celem oceny struktur podzastawkowych. Kalibratory 1173B i 1173R są oznaczone rozmiarem bioprotezy.

Krok	Postępowanie
1	**Ustalanie wymiarów za pomocą kalibratora cylindra 1173B:** Aby ustalić wymiary za pomocą kalibratora cylindra 1173B, należy przełożyć część cylindryczną kalibratora przez pierścień zastawki mitralnej. Upewnić się, że część cylindryczna jest położona bezpośrednio w płaszczyźnie pierścienia zastawki mitralnej. HVT60 
2	**Ustalanie wymiarów za pomocą kalibratora 1173R:** Aby ustalić wymiary za pomocą kalibratora 1173R, należy przeprowadzić część cylindryczną kalibratora przez pierścień zastawki mitralnej w taki sposób, aby końcówka kalibratora (symulująca część pierścienia do wszywania bioprotezy) spoczywała na górnej krawędzi pierścienia. HVT61 

Inne techniki, jak zastosowanie podkładek, fałdowanie (reefing) płatków lub zachowywanie mitralnego aparatu podzastawkowego mogą dodatkowo zmniejszać rozmiar pierścienia zastawki mitralnej, a tym samym rozmiar bioprotezy do wszczepienia (poz. 8). Przy stosowaniu tych technik zaleca się ponownie określić rozmiar pierścienia dla uniknięcia wszczepienia zbyt dużej bioprotezy. Spójna wydolność osierdziowych bioprotez mitralnych Edwards model 11000M czyni wszczepianie zbyt dużego rozmiaru protezy niepotrzebnym do osiągnięcia pożądanej wydolności hemodynamicznej u większości pacjentów (tabela 11 i 12).

Ze względu na elastyczne właściwości struna może zostać wydłużona przez system uchwytu Tricentrix podczas implantacji, jednak skurczy się po usunięciu uchwytu, chwytając płatki i zaburzając funkcję zastawki. Kalibratory 1173B i 1173R są wykonane z przezroczystego materiału, aby aparat podzastawkowy był widoczny podczas dobierania rozmiaru. Należy upewnić się, że żadna ze strun nie znajdzie się na drodze rozpórek.

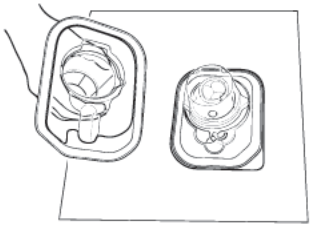
Przestroga: Przy stosowaniu technik zachowania aparatu podzastawkowego należy zachować szczególną ostrożność, aby nie doszło do uchwycenia strun ścięgnistych w rozpórce.

Ostrzeżenie: Unikać stosowania zbyt dużego rozmiaru bioprotezy. Stosowanie zbyt dużego rozmiaru może spowodować uszkodzenie bioprotezy lub miejscowe naprężenia mechaniczne, których skutkiem może być uszkodzenie serca, zniszczenie tkanki płatków, zniekształcenie stentu i przepływ fali zwrotnej.

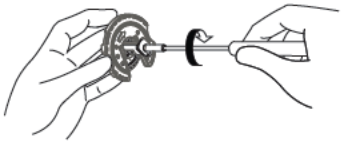
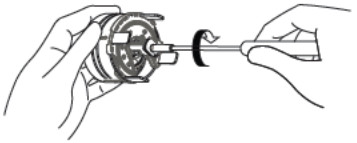
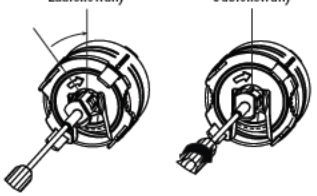
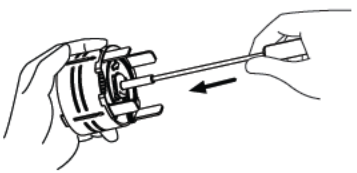
10.3 Instrukcje dotyczące manipulacji i przygotowania

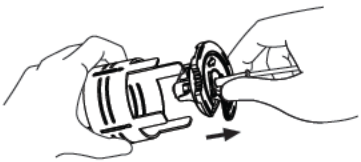
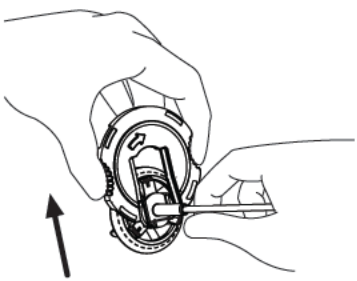
Zaleca się przeprowadzenie szkolenia w miejscu pracy przed rozpoczęciem manipulacji i przygotowania osierdziowej bioprotezy mitralnej Edwards, model 11000M.

Krok	Postępowanie
1	**Przestroga: Nie otwierać opakowania osierdziowej bioprotezy mitralnej Edwards model 11000M przed upewnieniem się, że dojdzie do implantacji.** **Ostrzeżenie: Nie otwierać torebki foliowej w polu jałowym. Torebka foliowa stanowi jedynie osłonę zabezpieczającą. Jedynie najbardziej wewnętrzne opakowanie tacowe można wprowadzać do pola jałowego.** Po wyborze odpowiedniego rozmiaru bioprotezy należy, poza polem jałowym, wyjąć z kartonu torebkę foliową. Przed otwarciem należy sprawdzić, czy opakowanie nie jest uszkodzone i czy nie brakuje pieczęci lub czy nie są one uszkodzone.
2	Należy przytrzymać podstawę tacy zewnętrznej w pobliżu pola jałowego i oderwać pokrywę tacy zewnętrznej.

Krok	Postępowanie
3	Taca wewnętrzna i jej zawartość są jałowe. Należy przełożyć tacę wewnętrzną do pola jałowego. Przy postępowaniu z wewnętrzną tacą należy stosować jałowe techniki chirurgiczne w celu uniknięcia skażenia. HVT26 
4	**Przestroga: Nie otwierać wewnętrznego opakowania przed upewnieniem się, że dojdzie do implantacji, a także dopóki chirurg nie przygotuje się do umieszczenia zastawki.** **Przestroga: Bioproteza nie jest przymocowana do tacy wewnętrznej. Należy ostrożnie odrywać pokrywę i usuwać plastikową osłonę.** Przed otwarciem należy sprawdzić, czy taca wewnętrzna i pokrywa nie są uszkodzone, poplamione i czy nie brakuje pieczęci lub czy nie są one uszkodzone. Należy przytrzymać podstawę tacy wewnętrznej i oderwać pokrywę tacy wewnętrznej.
5	Aby uzyskać dostęp do bioprotezy, należy usunąć plastikową osłonę przez pociągnięcie za obie zakładki. Wyrzucić plastikową osłonę. HVT58  HVT54 

Krok	Postępowanie
6	Przymocować rękojeść do systemu uchwytu Tricentrix, gdy bioproteza znajduje się jeszcze na tacy. W celu połączenia należy włożyć rękojeść do uchwytu i obracać zgodnie z ruchem wskazówek zegara do momentu napotkania wyraźnego oporu. HVT52  **Przestroga: Bioprotezy nie należy chwytać rękoma ani za pomocą narzędzi chirurgicznych.** **Przestroga: Należy zwrócić uwagę, by w trakcie mocowania nie dopuścić do zaplątania etykiety z numerem seryjnym wokół rękojeści.** **Przestroga: Zespół rękojeść/uchwyt jest potrzebny w trakcie implantacji i nie należy go usuwać do momentu przyszycia bioprotezy do pierścienia.**
7	Po zamocowaniu rękojeści wyjąć cały zespół (tj. plastikowy rękaw, zaczep, system uchwytu Tricentrix i bioprotezę) z tacy. Rękaw plastikowy jest luźno nałożony na zacisk i może pozostać na tacy. Nie wpłynie to na stosowanie produktu. HVT53 

Krok	Postępowanie
	Uchwyciwszy plastikowy rękaw lub zacisk, kontynuować rotację w celu przezwyciężenia oporu do momentu, gdy biały słupek uchwytu znajdzie się w pozycji odblokowanej. CP1089-23  Lub CP1089-6  CP1089-8 CP1089-9 Zablokowany Odblokowany 
8	Należy nacisnąć z wymaganą siłą uchwyt, tak aby biały słupek uchwytu wsunął się między płatki i zablokował się w ostatecznej pozycji otwartej. Osiągnięcie ostatecznej pozycji jest sygnalizowane odgłosem kliknięcia. CP1089-24 

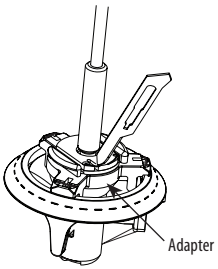
Krok	Postępowanie
9	**Przestroga: Jeżeli podczas otwierania systemu uchwytu Tricentrix nie popchnięto rękojeści z odpowiednią siłą, układ namiotowy nie będzie zabezpieczony i nie będzie w stanie zminimalizować możliwości uchwycenia szwów.** Zawsze należy sprawdzać właściwe rozstawienie. Pomiędzy niebieskim adapterem i szarym uchwytem nie powinno być wolnego miejsca. Zespół uchwyt-słupek nie powinien być w stanie się dalej przesuwać. Biały słupek uchwytu powinien wystawać przez płatki, podczas gdy trzy spoidła powinny być lekko odchylone w stronę centralnej części bioprotezy. Płatki będą chwilowo zmarszczone przez opuszczony biały słupek uchwytu. Po wyjęciu uchwytu po wszczepieniu płatki powrócą do normalnej pozycji. HVT56 
10	Po opuszczeniu wyjąć rękaw (jeżeli jest przyłączony) przez przytrzymanie rękojeści i wyciągnięcie rękawa z zacisku. CP1089-25 
11	Zdjąć zacisk przez zsunięcie go z uchwytu w kierunku bocznym. CP1089-26  Należy wyrzucić rękaw i zacisk.

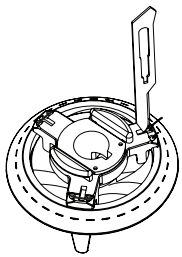
Krok	Postępowanie
12	Do każdego pierścienia do wszywania bioprotezy dołączona jest etykieta z numerem seryjnym. Należy sprawdzić, czy numer seryjny jest zgodny z numerem na opakowaniu bioprotezy i kartą danych implantacji bioprotezy. Etykiety nie należy odrywać od bioprotezy przed upewnieniem się, że dojdzie do wszczepienia. **Przestroga: W przypadku zauważenia jakiejkolwiek różnicy w numerze seryjnym należy zwrócić nieużywaną bioprotezę.** **Przestroga: Należy zwrócić szczególną uwagę na to, aby podczas usuwania etykiety z numerem seryjnym uniknąć nacięcia lub rozerwania tkaniny pierścienia do wszywania.** **Przestroga: By uniknąć uszkodzenia tkaniny pierścienia do wszywania, nie należy przeciągać supła szwu z etykietą z numerem seryjnym przez pierścień do wszywania.**
13	Osierdziowa bioproteza mitralna Edwards model 11000M **NIE WYMAGA PŁUKANIA** przed implantacją. **Przestroga: Jeśli bioproteza zostanie wypłukana przed implantacją, należy ją utrzymywać w stanie nawodnienia jałowym roztworem soli fizjologicznej po obu stronach tkanki płatka przez pozostały czas trwania zabiegu chirurgicznego. Zaleca się przepłukiwanie co jedną lub dwie minuty.** **Przestroga: Należy unikać kontaktu tkanki płatka z ręcznikami, płótnem i innymi źródłami materii pylastej, która może zostać przeniesiona na tkankę płatka.**

10.4 Implantacja urządzenia

Krok	Postępowanie
1	Chirurg powinien znać zalecenia dotyczące doboru rozmiarów oraz umiejscowienia protezy ponad pierścieniem (Patrz 10.2 Kalibrowanie). Ze względu na złożoność i rodzaje operacji wymiany zastawki serca wybór techniki chirurgicznej, odpowiednio zmodyfikowanej zgodnie z wcześniej opisanymi **Ostrzeżeniami**, zależy od decyzji chirurga. Zasadniczo należy wykonać następujące kroki: 1. Chirurgicznie usunąć zmienione chorobowo lub uszkodzone płatki zastawki i wszystkie związane z nią struktury konieczne do usunięcia. 2. Chirurgicznie usunąć wapń z pierścienia w celu zapewnienia odpowiedniego umieszczenia pierścienia do wszywania bioprotezy i niedopuszczenia do uszkodzenia delikatnej tkanki płatka. 3. Odpowiednio dobrać rozmiar. Zmierzyć pierścień, posługując się wyłącznie modelami kalibratorów mitralnych 1173B i 1173R (Rysunki 1a-1b). 4. Prawidłowo osadzić protezę. 5. Założyć szwy z umieszczonym na miejscu uchwytem w celu zminimalizowania możliwości zapętlenia szwów lub uchwycenia strun ścięgnistych.

Krok	Postępowanie
	6. Upewnić się, że nie nastąpiło uszkodzenie płatków bioprotezy podczas zakładania szwów i że nie występuje przeciek. **Przestroga: Podczas doboru wymiarów bioprotezy dla danego pacjenta należy wziąć pod uwagę jego wymiary anatomiczne, wiek i kondycję fizyczną, aby zmniejszyć do minimum możliwość uzyskania suboptymalnego wyniku hemodynamicznego. Jednak ostatecznego doboru bioprotezy w poszczególnych przypadkach powinien dokonać lekarz po starannym rozważeniu wszystkich zagrożeń i korzyści dla określonego pacjenta.** **Przestroga: Przed implantacją protezy należy w dostatecznym stopniu usunąć złogi wapnia z pierścienia włóknistego u pacjenta, aby uniknąć uszkodzenia delikatnych płatków bioprotezy w wyniku ich kontaktu ze złogami wapnia. Należy wprowadzić kalibrator do pierścienia zastawki mitralnej. Cylinder kalibratora powinien zawsze mieścić się swobodnie w pierścieniu.** **Przestroga: Do wyboru rozmiaru bioprotezy stosować wyłącznie kalibratory 1173B lub 1173R; inne kalibratory mogą prowadzić do wyboru niewłaściwej zastawki (patrz 1.2 Opis akcesoriów). Podobnie do innych bioprotez mitralnych, osierdziową bioprotezę mitralną Edwards model 11000M wszczepia się zazwyczaj za pomocą zakładkowych szwów materacowych. Zaleca się dokonanie pomiaru pierścienia po założeniu szwów, ponieważ mogą one zmniejszyć rozmiar bioprotezy przeznaczonej do wszczepienia.**
2	**Prawidłowe zorientowanie bioprotezy:** **Przestroga: Rama prowadnicy drucianej bioprotezy model 11000M jest symetryczna, a trzy podpórki spoidła (rozpórki) są rozmieszczone w równych odstępach. Jednak pierścień do wszywania został tak zaprojektowany, aby można go było użyć w określonym położeniu bioprotezy. Obrębiona część pierścienia do wszywania, znajdująca się pomiędzy dwoma silikonowymi wybrzuszeniami, powinna być umieszczona naprzeciw przedniej międzyspoidłowej części pierścienia, obejmując drogę odpływu z lewej komory.** Kontrastujące szwy znacznikowe na pierścieniu do wszywania są przeznaczone do ułatwienia właściwego ułożenia i wskazują typową odległość międzyspoidłową. Jednak odległość ta może różnić się u poszczególnych pacjentów. Po lewej stronie, dwa sąsiadujące ze sobą czarne szwy wskazują miejsce, w którym powinien być wykonany pierwszy szew i odzwierciedlają spoidło przednie. Po prawej stronie pojedynczy czarny szew wskazuje przybliżoną lokalizację spoidła tylnego. Dzięki wykorzystaniu powyższych pomocy w ułożeniu trzeci element powinien w sposób naturalny wypaść w miejscu (lub w pobliżu) tylnego płatka. **Przestroga: Należy zwrócić szczególną uwagę, aby nie umieścić rozpórki na wprost drogi odpływu z lewej komory, ponieważ mogłoby to upośledzić długookresową wydolność hemodynamiczną.**

Krok	Postępowanie
3	**Założenie szwu:** Czarna linia prowadząca szew obiega pierścień do wszywania. Przy zakładaniu szwów na pierścieniu do wszywania można zredukować siły przesuwające pierścień przez rozmieszczanie szwów na wprost przez pierścień i w obszarze od linii prowadzącej szwy do zewnętrznej części pierścienia do wszywania. Należy utrzymywać szwy naprężone podczas obniżania bioprotezy do pierścienia; minimalizuje to możliwość utworzenia się zapętleń szwu, które mogłyby uchwycić płatek. Wraz z w pełni wsuniętymi wspornikami stentu, gdy system uchwytu Tricentrix znajduje się na miejscu, pomaga to we wprowadzeniu szwów do ich właściwych pozycji poza rozpórkami oraz na pierścieniu do wszywania. Przed zawiązaniem szwów należy usunąć rękojeść. Rękojeść i niebieski adapter muszą zostać usunięte razem jako zespół. Utrzymać rozmieszczenie bioprotezy w obrębie pierścienia przez delikatne chwycenie uchwytu kleszczykami lub dłonią w rękawiczce i przecięcie zielonej nitki na niebieskim adapterze. Zestaw niebieskiego adaptera i rękojeści należy wyjąć w całości jako zespół. CP1089-27 
4	**Przestroga: Należy unikać zapętlenia lub uwięzienia szwu wokół otwartych elementów szkieletu, wolnych rozpórek lub wsporników spoideł bioprotezy, co mogłoby zakłócać prawidłowe działanie zastawki. Dla zminimalizowania ryzyka zapętlenia szwów należy koniecznie pozostawić uchwyt w sercu do momentu zakończenia szycia.** Jeżeli jednak pozostawienie uchwytu na miejscu ogranicza pole widzenia chirurga, wszystkie szwy przylegające do każdej z trzech rozpórek szkieletu muszą zostać związane przed przecięciem trzech zielonych nici utrzymujących uchwyt (w celu jego usunięcia). **Przestroga: Jeżeli szwy utrzymujące umieszczony uchwyt zostaną przecięte przed związaniem tych przylegających szwów, uchwyt nie będzie już minimalizować możliwości zapętlenia szwów wokół rozpórek szkieletu.**

Krok	Postępowanie
	Należy w szczególności uważać, aby nie zawiązać szwów na szczytach rogów szarych odnóg uchwytu. Przed zawiązaniem każdego ze szwów trzeba sprawdzić płatki, utrzymując oba końce nici w stanie naprężenia. Odkształcenie lub ruch płatków podczas tej czynności może świadczyć o zapętleniu szwu wokół rozpórki. W żadnym momencie przed usunięciem uchwytu lub po jego usunięciu nie wolno zmniejszyć naprężenia nici, gdyż mogłoby to spowodować powstanie pętli na szwach i ewentualnie uwięzienie. Zaleca się umieszczenie lusterka chirurgicznego za płatkami po usunięciu uchwytu, aby sprawdzić każdą rozpórkę i właściwe umieszczenie szwów. **Przestroga: Podczas zakładania szwów przerywanych istotne jest, aby uciąć nici blisko punktów wiązania i upewnić się, aby odsłonięte końcówki nici nie stykały się z tkanką płatków (poz. 8).** System uchwytu Tricentrix usuwa się jako jedną część po zakończeniu zakładania szwów w następujący sposób: CP1089-14  1. Należy przeciąć każdy z trzech (3) widocznych zielonych szwów, używając skalpela lub nożyczek wprowadzonych wyłącznie do kanału cięcia. Nigdy nie wolno podejmować prób przecięcia szwów pod częściowo oddzielonym uchwytem, ponieważ część szwów mocujących może wpaść do komory serca. Należy unikać przecięcia oraz uszkodzenia stentu lub tkanki płatków podczas przecinania szwów. 2. Po prawidłowym przecięciu wszystkich trzech (3) szwów mocujących należy usunąć z bioprotezy (jako jedną część) system uchwytu Tricentrix wraz ze szwami mocującymi, używając jałowych rękawic lub zabezpieczonych kleszczyków. 3. Po implantacji wyjąć i wyrzucić uchwyt.

10.5 Czyszczenie i sterylizacja akcesoriów

Akcesoria do osierdziowej bioprotezy mitralnej Edwards, model 11000M, są pakowane oddzielnie. Rękojeść model 1126 dostarczana jest w stanie jałowym i jest przeznaczona wyłącznie do jednorazowego użytku. Rękojeści model 1111, 1117 i 1173 oraz kalibratory model 1173B i 1173R są dostarczane w stanie niejałowym i przed użyciem trzeba je umyć i wyjałowić. Należy wyczyścić i ponownie wysterylizować rękojeści, kalibratory, podstawę i pokrywę tacy przed każdym użyciem. Instrukcje dotyczące mycia i wyjaławiania zawarte są w instrukcji stosowania dostarczanej z akcesoriami wielorazowymi.

10.6 Zwrot bioprotez

Firma Edwards Lifesciences jest zainteresowania otrzymaniem odzyskanych klinicznych egzemplarzy osierdziowej bioprotezy mitralnej model 11000M do analizy. W celu zwrotu odzyskanych bioprotez należy skontaktować się z lokalnym przedstawicielem firmy.

- Nieotwarte opakowanie z nienaruszoną barierą jałową: Jeśli torebka foliowa ani tace nie zostały otwarte, bioprotezę należy zwrócić w oryginalnym opakowaniu.
- Otwarte opakowanie, lecz bioproteza nie została wszczepiona: Jeśli taca została otwarta, bioproteza nie jest już jałowa. Jeśli bioproteza nie zostanie wszczepiona, należy ją umieścić w odpowiednim utrwalaczu histologicznym, takim jak 10% formalina lub 2% aldehyd glutarowy, i zwrócić do firmy. W takich okolicznościach schłodzenie nie jest konieczne.
- Eksplantowana bioproteza: Usunięte bioprotezy należy umieszczać w odpowiednim utrwalaczu histologicznym, takim jak 10% formalina czy 2% aldehyd glutarowy, a następnie zwrócić do firmy. W takich okolicznościach schłodzenie nie jest konieczne.

11. Zasady bezpieczeństwa w środowisku rezonansu magnetycznego (MR)

Warunki w badaniu MR

Badania pozakliniczne wykazały, że osierdziowa bioproteza mitralna Edwards model 11000M może być stosowana w środowisku MR. Pacjent z bioprotezą zastawki mitralnej 11000M może być bezpiecznie skanowany bezpośrednio po umieszczeniu implantu przy zachowaniu następujących warunków:

- Statyczne pole magnetyczne o indukcji nieprzekraczającej 3 tesli.
- Maksymalny gradient przestrzenny pola wynoszący 720 gausów/cm.
- Maksymalny raportowany w systemie MR, uśredniony dla całego ciała współczynnik absorpcji promieniowania (SAR) wynosi 3 W/kg na 15 minut skanowania.

W badaniach pozaklinicznych osierdziowa bioproteza mitralna Edwards model 11000M wywołała wzrost temperatury o nie więcej niż o 0,5°C przy maksymalnym raportowanym w systemie MR, uśrednionym dla całego ciała współczynniku absorpcji promieniowania (SAR) wynoszącym 3 W/kg na 15 minut skanowania MR w systemie o indukcji 3 T (Excite, Software G3.0-052B, General Electric Healthcare).

Jakość obrazu MR może być nieprawidłowa, jeżeli obszar badania mieści się w tym samym obszarze lub blisko bioprotezy mitralnej 11000M. Zalecana jest optymalizacja parametrów obrazowania MR.

12. Informacje dla pacjentów

12.1 Karta identyfikacyjna badania

Karta identyfikacyjna badania jest przekazywana każdemu pacjentowi ze wszczepioną osierdziową protezą mitralną Edwards model 11000M.

12.2 Materiały informacyjne dla pacjenta

Materiały informacyjne dla pacjenta można uzyskać w firmie Edwards lub u przedstawiciela klinicznego firmy Edwards.

13. Piśmiennictwo

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Ceny mogą ulec zmianie bez powiadomienia. Niniejszy produkt jest wytwarzany i sprzedawany zgodnie z co najmniej jednym spośród następujących patentów amerykańskich: nr patentu w USA 5,928,281; 5,931,969; 5,961,549; 6,102,944; 6,245,105; 6,413,275; 6,416,547; 6,561,970; 6,585,766; 6,837,902; 6,945,997; 6,966,925; RE 40570; 7,214,344; 7,658,763; 7,682,391; 7,972,376; 8,007,992; 8,357,387 oraz 8,632,608; i odpowiadających im patentów zarejestrowanych za granicą. Ponadto trwa uzyskiwanie innych patentów.

Należy zapoznać się z objaśnieniami symboli, umieszczonymi na końcu niniejszego dokumentu.

Tabela 3: Zaobserwowane częstotliwości zdarzeń niepożądanych – MVR i DVR (Model 6900)

Wszyscy pacjenci poddani analizie: N = 363 Skumulowana liczba obserwacji: 1100 pacjentolat

Powikłanie	Zdarzenia wczesne		Zdarzenia późne[1]		Bez zdarzeń niepożądanych (%) [95% CI][2]		
	n[3]	%	n	%/pacjentorok	1 rok (n = 287)	5 lat (n = 141)	8 lat (n = 18)
Śmiertelność (całkowita)	34	9,4	50	4,7	85,5 [81,8; 89,2]	75,4 [70,3; 80,6]	65,4 [57,6; 73,2]
Zdarzenia związane z zastawką							
Śmiertelność (związana z zastawką)	0	0	16	1,5	97,7 [96,0; 99,4]	95,3 [92,8; 97,8]	91,9 [87,5; 96,4]
Eksplantacje	0	0	8	0,7	98,7 [98,0; 99,3]	96,7 [95,3; 98,0]	95,6 [93,9; 97,3]
Powtórne operacje	2	0,6	12	1,1	97,1 [96,2; 98,1]	95,1 [93,6; 96,6]	93,0 [90,9; 95,1]
Krwotok związany z antykoagulacją	2	0,6	9	0,8	97,1 [95,2; 99,0]	97,1 [95,2; 99,0]	94,1 [88,2; 100]
Zapalenie wsierdzia	1	0,3	3	0,3	99,0 [97,9; 100]	98,7 [97,4; 98,9]	98,7 [97,4; 98,9]
Hemoliza	0	0,0	1	0,1	99,7 [99,0; 100]	99,7 [99,0; 100]	99,7 [99,0; 100]
Dysfunkcja pozastrukturalna	0	0,0	3	0,3	100 [100; 100]	99,3 [98,0; 100]	98,3 [95,9; 100]
Przeciek okołozastawkowy (wszystkie)	1	0,3	5	0,5	98,4 [97,0; 99,8]	98,4 [97,0; 99,8]	97,3 [94,9; 99,8]
Strukturalne pogorszenie stanu zastawki	0	0,0	5	0,5	100,0 [100; 100]	97,6 [95,2; 100]	92,8 [85,3; 100]
Zaburzenia zakrzepowo-zatorowe	5	1,4	8	0,7	97,5 [95,8; 99,2]	96,1 [93,8; 98,5]	96,1 [93,8; 98,5]
Zakrzepica	0	0,0	0	0,0	100,0 [100; 100]	100,0 [100; 100]	100,0 [100; 100]

Uwagi:

1. Częstości zdarzeń późnych zostały obliczone jako częstości przedstawione liniowo (%/pacjentorok) w oparciu o 1072,5 późnych pacjentolat (> 30 dni po zabiegu).
2. Przebieg bez zdarzeń niepożądanych został obliczony przy użyciu metody Kaplana-Meiera. Do obliczenia standardowego błędu tych zmiennych zastosowany został wzór Greenwooda.
3. n = liczba zdarzeń.

Tabela 4: Zaobserwowane częstotliwości zdarzeń niepożądanych (Model 6900P)

Wszyscy pacjenci poddani analizie: N = 209 Skumulowana liczba obserwacji: 873,18 pacjentolat ogółem

Powikłanie	Zdarzenia wczesne		Zdarzenia późne[1]		Bez zdarzeń niepożądanych (%) [95% CI][2]	
	n[3]	%	n	%/pacjentorok	1 rok	5 lat
Śmiertelność (całkowita)	3	1,4	45	5,3	93,2 [88,8; 95,9]	74,4 [66,9; 80,5]
Zdarzenia związane z zastawką						
Śmiertelność (związana z zastawką)	1	0,5	12	1,4	98,5 [95,5; 99,5]	92,0 [86,2; 95,5]
Eksplantacje	1	0,5	8	0,9	97,5 [94,0; 98,9]	96,5 [92,2; 98,5]
Powtórne operacje	0	0,0	0	0,0	100,0 [100; 100]	100,0 [100; 100]
Zdarzenia związane z krwawieniem	5	2,4	13	1,5	96,1 [92,3; 98,0]	91,9 [86,5; 95,2]
Zapalenie wsierdzia	1	0,5	3	0,4	99,5 [96,6; 99,9]	97,1 [92,1; 98,9]
Dysfunkcja pozastrukturalna	0	0,0	1	0,1	99,5 [96,4; 99,9]	99,5 [96,4; 99,9]
Przeciek okołozastawkowy (wszystkie)	1	0,5	2	0,2	99,5 [96,7; 99,9]	98,4 [95,2; 99,5]
Strukturalne pogorszenie stanu zastawki	0	0,0	2	0,2	100,0 [100; 100]	99,0 [93,2; 99,9]
Zaburzenia zakrzepowo-zatorowe	4	1,9	12	1,4	97,0 [93,5; 98,7]	91,3 [85,8; 94,7]
Zakrzepica	0	0,0	0	0,0	100,0 [100; 100]	100,0 [100; 100]

Uwagi:

1. Częstości zdarzeń późnych zostały obliczone jako częstości przedstawione liniowo (%/pacjentorok) w oparciu o 856,24 późnych pacjentolat (> 30 dni po zabiegu).
2. Przebieg bez zdarzeń niepożądanych został obliczony przy użyciu metody Kaplana-Meiera. Do obliczenia standardowego błędu tych zmiennych zastosowany został wzór Greenwooda.
3. n = liczba zdarzeń.

Tabela 5: Przedoperacyjne dane demograficzne pacjentów (Model 6900)

Parametr	Kategoria	Charakterystyka badania (N = 363; łącznie 1100 pacjentolat)	
		n	% (n/N)[1]
Wiek w momencie wszczepienia (N = 363)	Średnia ± SD	66,1 ± 10,7	
Płeć	Kobieta/mężczyzna	212/151	58,4%/41,6%
Rozpoznanie/etiologia	Brak	30	8,3%
	Stenoza	91	25,1%
	Niedomykalność	184	50,7%
	Wada złożona	58	16,0%

Uwaga:

1. n = liczba pacjentów w każdej kategorii; N = liczba pacjentów w badaniu ogółem.

Tabela 6: Przedoperacyjne dane demograficzne pacjentów (Model 6900P)

Parametr	Kategoria	Charakterystyka badania (N = 209; łącznie 873,18 pacjentolat)	
		n	% (n/N)[1]
Wiek w momencie wszczepienia (N = 209)	Średnia ± SD	71,4 ± 9,4	
Płeć	Kobieta/mężczyzna	138/71	66,0%/34,0%
Rozpoznanie/etiologia	Wada złożona	48	23,0%
	Niedomykalność	121	57,9%
	Stenoza	32	15,3%
	Dysfunkcja zastawki	8	3,8%

Uwaga:

1. n = liczba pacjentów w każdej kategorii; N = liczba pacjentów w badaniu ogółem.

Tabela 7: Operacyjne dane demograficzne pacjentów (Model 6900)

		Charakterystyka badania (N = 363; łącznie 1100 pacjentolat)	
Parametr	Kategoria	n	% (n/N)[1]
Etiologia[2]	Choroba reumatyczna serca	135	37,2%
	Zwapnienie	82	22,6%
	Degeneracja	50	13,8%
	Zapalenie wsierdzia	39	10,7%
	Uszkodzenie bioprotezy	15	4,1%
	Choroba niedokrwienna serca	14	3,9%
	Nieprawidłowości wrodzone	8	2,2%
	Inna	44	12,1%
Procedury towarzyszące[2]	Brak	200	55,1%
	CABG[3]	78	21,5%
	Zabieg naprawczy zastawki trójdzielnej	61	16,8%
	Kontrapulsacja wewnątrzaortalna	17	4,7%
	Rozrusznik[4]	6	1,7%
	Zabieg naprawczy aorty/wymiana	5	1,4%
	Zabieg naprawczy tętniaka	4	1,1%
	Inna	31	8,5%
Występujące wcześniej schorzenia[2]	Brak	122	33,6%
	CAD[5]/CABG	72	19,8%
	Nadciśnienie	61	16,8%
	Migotanie przedsionków	53	14,6%
	Przebyty MI[6]	45	12,4%
	Choroba naczyń mózgowych	36	9,9%
	Inna	234	64,5%
Rozmiar zastawki (mm)	25	22	6,1%
	27	110	30,3%
	29	137	37,7%
	31	81	22,3%
	33	13	3,6%

Uwagi:

1. n = liczba pacjentów w każdej kategorii; N = liczba pacjentów w badaniu ogółem
2. Może być więcej niż jeden na pacjenta
3. CABG = Coronary Artery Bypass Graft (Pomostowanie aortalno-wieńcowe)
4. Utrwalone lub napadowe
5. CAD = Coronary Artery Disease (Choroba wieńcowa)
6. MI = Myocardial Infarction (Zawał serca)

Tabela 8: Operacyjne dane demograficzne pacjentów (Model 6900P)

		Charakterystyka badania (N = 209; łącznie 873,18 pacjentolat)	
Parametr	Kategoria	n	% (n/N)[1]
Etiologia[2]	Zwapnienie	38	18,2%
	Wada wrodzona	1	0,5%
	Zmiany zwyrodnieniowe	105	50,2%
	Odległe następstwa zapalenia wsierdzia	10	4,8%
	Niedokrwienne	12	5,7%
	Reumatyczne	64	30,6%
	Inna	36	17,2%
Procedury towarzyszące[2]	Brak	91	43,5%
	Korekta zastawki/pierścienia włóknistego	3	1,4%
	CABG[3]	58	27,8%
	Stały stymulator serca	1	0,5%
	Korekta zastawki trójdzielnej/pierścienia włóknistego	21	10,0%
	Inna	78	37,3%
Występujące wcześniej schorzenia[2]	Brak	17	8,1%
	Arytmie	95	45,5%
	CAD[4]	85	40,7%
	Kardiomiopatia	13	6,2%
	Zastoinowa niewydolność serca	66	31,6%
	Zapalenie wsierdzia	14	6,7%
	Zawał mięśnia sercowego	21	10,0%
	Choroba naczyń obwodowych	9	4,3%
	Nadciśnienie płucne	66	31,6%
	Gorączka reumatyczna	16	7,7%
	Nadciśnienie uogólnione	49	23,4%
	TIA[5]/CVA[6]	24	11,5%
	Inna	35	16,7%
Rozmiar zastawki (mm)	25	28	13,4%
	27	37	17,7%
	29	84	40,2%
	31	43	20,6%
	33	17	8,1%

Uwagi:

1. n = liczba pacjentów w każdej kategorii; N = liczba pacjentów w badaniu ogółem
2. Może być więcej niż jeden na pacjenta
3. CABG = Coronary Artery Bypass Graft (Pomostowanie aortalno-wieńcowe)
4. CAD = Coronary Artery Disease (Choroba wieńcowa)
5. TIA = przejściowy atak niedokrwienny
6. CVA = udar mózgu

Tabela 9: Skuteczność według kryterium klasyfikacji NYHA (Model 6900)

	Ocena przedoperacyjna		Oceny pooperacyjne			
			1 do 2 lat		5 lat	
Klasa funkcjonalna NYHA	n/N[1]	%	n/N	%	n/N	%
I	11/363	3,0	120/268	44,8	40/129	31,0
II	73/363	20,1	90/268	33,6	25/129	19,4
III	192/363	52,9	15/268	5,6	1/129	0,8
IV	84/363	23,1	0/268	0,0	0/129	0,0
Niedostępne	3/363	0,8	43/268	16,0	63/129	48,8

Uwaga:

1. n = liczba pacjentów w każdej kategorii; N = liczba pacjentów w badaniu ogółem.

Tabela 10: Skuteczność według kryterium klasyfikacji NYHA (Model 6900P)

	Ocena przedoperacyjna		Oceny pooperacyjne			
			1 rok		5 lat	
Klasa funkcjonalna NYHA	n/N[1]	%	n/N	%	n/N	%
I	6/209	2,9	86/187	46,0	30/96	31,3
II	27/209	12,9	68/187	36,4	33/96	34,4
III	121/209	57,9	8/187	4,3	6/96	6,3
IV	55/209	26,3	1/187	0,5	0/96	0,0
Niedostępne	0/209	0,0	24/187	12,8	27/96	28,1

Uwaga:

1. n = liczba pacjentów w każdej kategorii; N = liczba pacjentów w badaniu ogółem.

Tabela 11: Skuteczność, wyniki badań hemodynamicznych[1] (Model 6900)

Parametr hemodynamiczny	Wyniki w zależności od rozmiaru zastawki				
	25 mm	27 mm	29 mm	31 mm	33 mm
Przy wypisie/krótko po implantacji (n = 130, 109 MVR[2] i 21 DVR[3])					
Średni gradient[4]	n = 3	n = 23	n = 36	n = 23	n = 3
• Średnia ± SD	5,7 ± 1,2	4,2 ± 1,7	4,2 ± 1,7	3,6 ± 1,0	7,5 ± 5,8
• min., maks.	5, 7	2, 9	1, 8	2, 5	3, 14
EOA[5]	n = 1	n = 17	n = 22	n = 25	n = 5
• Średnia ± SD	1,5	2,9 ± 0,9	3,1 ± 0,9	2,5 ± 0,7	3,0 ± 1,2
• min., maks.	1,5; 1,5	1,3; 4,1	1,4; 4,2	1,5; 3,8	1,6; 4,9
Fala zwrotna[6]	n = 3	n = 28	n = 51	n = 40	n = 8
0	3/3 (100%)	22/28 (79%)	36/51 (71%)	30/40 (75%)	4/8 (50%)
1+	0/3 (0%)	5/28 (18%)	13/51 (25%)	7/40 (18%)	4/8 (50%)
2+	0/3 (0%)	0/28 (0%)	1/51 (2%)	3/40 (7%)	0/8 (0%)
3+	0/3 (0%)	0/28 (0%)	1/51 (2%)	0/40 (0%)	0/8 (0%)
4+	0/3 (0%)	0/28 (0%)	0/51 (0%)	0/40 (0%)	0/8 (0%)
Niedostępne	0/3 (0%)	1/28 (3%)	0/51 (0%)	0/40 (0%)	0/8 (0%)
3–6 miesięcy po implantacji (n = 49, 42 MVR[2] i 7 DVR[3])					
Średni gradient[4]	n = 5	n = 19	n = 15	n = 5	n = 2
• Średnia ± SD	6,4 ± 1,7	5,3 ± 5	3,4 ± 1,2	4 ± 1,9	4 ± 0
• min., maks.	5, 9	2, 25	2, 6	2, 7	4, 4
EOA[5]	n = 5	n = 18	n = 13	n = 5	n = 2
• Średnia ± SD	2,9 ± 0,8	2,6 ± 0,7	2,8 ± 0,6	2,9 ± 0,3	2,6 ± 1
• min., maks.	1,8; 3,6	1,5; 5	2; 3,8	2,4; 3,3	2; 3,3
Fala zwrotna[6]	n = 5	n = 21	n = 15	n = 6	n = 2
0	3/5 (60%)	17/21 (81%)	6/15 (40%)	4/6 (67%)	1/2 (50%)
1+	0/5 (0%)	4/21 (19%)	8/15 (53%)	2/6 (33%)	0/2 (0%)
2+	1/5 (20%)	0/21 (0%)	1/15 (7%)	0/6 (0%)	1/2 (50%)
3+	0/5 (0%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)
4+	1/5 (20%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)
Niedostępne	0/5 (0%)	0/21 (0%)	0/15 (0%)	0/6 (0%)	0/2 (0%)

Ciąg dalszy na następnej stronie.

Tabela 11: Skuteczność, wyniki badań hemodynamicznych[1] (Model 6900), ciąg dalszy

Parametr hemodynamiczny	Wyniki w zależności od rozmiaru zastawki				
	25 mm	27 mm	29 mm	31 mm	33 mm
1-2 lat po implantacji (n = 131, 114 MVR[2] i 17 DVR[3])					
Średni gradient[4]	n = 3	n = 40	n = 47	n = 27	n = 4
• Średnia ± SD	5,2 ± 0,7	4,1 ± 1,6	3,5 ± 1,8	3,1 ± 1,4	2,1 ± 0,5
• min., maks.	4,7; 6	1, 7	1, 10	1, 7	1,5; 2,7
EOA[5]	n = 2	n = 35	n = 46	n = 29	n = 5
• Średnia ± SD	1,8 ± 0,4	2,3 ± 0,6	2,6 ± 0,5	2,6 ± 0,7	2,5 ± 0,5
• min., maks.	1,5; 2,0	1,2; 3,5	1,1; 3,7	1,1; 3,7	2,1; 3,2
Fala zwrotna[6]	n = 4	n = 42	n = 51	n = 29	n = 5
0	2/4 (50%)	31/42 (74%)	36/51 (71%)	17/29 (59%)	3/5 (60%)
1+	1/4 (25%)	9/42 (21%)	11/51 (21%)	8/29 (27%)	1/5 (20%)
2+	1/4 (25%)	2/42 (5%)	4/51 (8%)	2/29 (7%)	1/5 (20%)
3+	0/4 (0%)	0/42 (0%)	0/51 (0%)	2/29 (7%)	0/5 (0%)
4+	0/4 (0%)	0/42 (0%)	0/51 (0%)	0/29 (0%)	0/5 (0%)
Niedostępne	0/4 (0%)	0/42 (0%)	0/51 (0%)	0/29 (0%)	0/5 (0%)
5 lat po implantacji (n = 11, 9 MVR[2] i 2 DVR[3])					
Średni gradient[4]	n = 0	n = 6	n = 5	n = 0	n = 0
• Średnia ± SD	nie dotyczy	8,8 ± 8,1	5,1 ± 2,3	nie dotyczy	nie dotyczy
• min., maks.	nie dotyczy	4, 25	3, 8	nie dotyczy	nie dotyczy
EOA[5]	n = 0	n = 2	n = 4	n = 0	n = 0
• Średnia ± SD	nie dotyczy	2,0 ± 1,5	2,9 ± 0,6	nie dotyczy	nie dotyczy
• min., maks.	nie dotyczy	1,0; 3,1	2,1; 3,5	nie dotyczy	nie dotyczy
Fala zwrotna[6]	n = 0	n = 6	n = 5	n = 0	n = 0
0	0/0 (0%)	4/6 (66%)	2/5 (40%)	0/0 (0%)	0/0 (0%)
1+	0/0 (0%)	1/6 (17%)	3/5 (60%)	0/0 (0%)	0/0 (0%)
2+	0/0 (0%)	1/6 (17%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
3+	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
4+	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)
Niedostępne	0/0 (0%)	0/6 (0%)	0/5 (0%)	0/0 (0%)	0/0 (0%)

Uwagi:

1. Oceny hemodynamiczne wykonane były z zastosowaniem przezklatkowego badania echokardiograficznego (TTE) oraz – w niektórych przypadkach – przezprzełykowego badania echokardiograficznego (TEE).
2. MVR = wymiana zastawki mitralnej
3. DVR = wymiana dwóch zastawek
4. Średni gradient wyrażony w mmHg
5. EOA: Efektywne pole ujścia, cm^2
6. Fala zwrotna = brak, 0; łagodna, 1+; umiarkowana, 2+; umiarkowana/ciężka, 3+; ciężka, 4+

Tabela 12: Skuteczność, wyniki badań hemodynamicznych (Model 6900P)[1]

Parametr hemodynamiczny	Wyniki w zależności od rozmiaru zastawki				
	25 mm	27 mm	29 mm	31 mm	33 mm
Przy wypisie/krótko po implantacji					
Średni gradient[2]	n = 24	n = 35	n = 83	n = 42	n = 16
• Średnia ± SD	6,4 ± 1,87	4,4 ± 1,52	3,4 ± 1,47	3,3 ± 1,20	4,0 ± 1,38
• min., maks.	3, 10	1,96; 8	1,4; 9	1, 7	1,5; 6,91
EOA[3]	n = 8	n = 27	n = 77	n = 41	n = 16
• Średnia ± SD	2,7 ± 0,87	2,8 ± 0,58	2,9 ± 0,93	2,5 ± 0,67	2,4 ± 0,52
• min., maks.	1,46; 4,4	1,5; 3,9	1,58; 6	1,32; 4,2	1,55; 3,31
Fala zwrotna[4]	n = 27	n = 37	n = 83	n = 43	n = 17
Nieznaczna/brak	19/27 (70%)	29/37 (78%)	76/83 (92%)	39/43 (91%)	15/17 (88%)
1+ łagodna	6/27 (22%)	7/37 (19%)	7/83 (8%)	4/43 (9%)	1/17 (6%)
2+ umiarkowana	1/27 (4%)	1/37 (3%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
3+ umiarkowana/ciężka	0/27 (0%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	1/17 (6%)
4+ ciężka	0/27 (0%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
Niedostępne	1/27 (4%)	0/37 (0%)	0/83 (0%)	0/43 (0%)	0/17 (0%)
3–6 miesięcy po implantacji					
Średni gradient[2]	n = 0	n = 4	n = 3	n = 2	n = 0
• Średnia ± SD	0 ± 0	4,4 ± 2,25	2,3 ± 0,89	6,6 ± 2,05	0 ± 0
• min., maks.	0, 0	2,5; 7,5	1,3; 3	5,1; 8	0, 0
EOA[3]	n = 0	n = 3	n = 3	n = 1	n = 1
• Średnia ± SD	0 ± 0	2,4 ± 0,74	3,2 ± 0,88	2,5 ± 0,00	1,2 ± 0,00
• min., maks.	0, 0	1,6; 3	2,3; 4,05	2,47; 2,47	1,22; 1,22
Fala zwrotna[4]	n = 0	n = 5	n = 3	n = 2	n = 2
Nieznaczna/brak	0	3/5 (60%)	2/3 (67%)	2/2 (100%)	2/2 (100%)
1+ łagodna	0	1/5 (20%)	1/3 (33%)	0/2 (0%)	0/2 (0%)
2+ umiarkowana	0	1/5 (20%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
3+ umiarkowana/ciężka	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
4+ ciężka	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)
Niedostępne	0	0/5 (0%)	0/3 (0%)	0/2 (0%)	0/2 (0%)

Ciąg dalszy na następnej stronie.

Tabela 12: Skuteczność, wyniki badań hemodynamicznych (Model 6900P)[1], ciąg dalszy

Parametr hemodynamiczny	Wyniki w zależności od rozmiaru zastawki				
	25 mm	27 mm	29 mm	31 mm	33 mm
1 rok po implantacji					
Średni gradient[2]	n = 16	n = 27	n = 63	n = 34	n = 15
• Średnia ± SD	5,9 ± 2,36	4,0 ± 1,45	3,0 ± 1,61	3,3 ± 1,26	3,4 ± 1,25
• min., maks.	3, 12	2, 7	1, 12	1,5; 7	1,9; 6,3
EOA[3]	n = 3	n = 21	n = 59	n = 32	n = 15
• Średnia ± SD	2,3 ± 0,16	2,4 ± 0,76	2,6 ± 0,74	2,5 ± 0,67	2,3 ± 0,83
• min., maks.	2,09; 2,4	1,27; 4,76	1,5; 5,7	1,5; 4	1,2; 3,8
Fala zwrotna[4]	n = 20	n = 28	n = 65	n = 34	n = 16
Nieznaczna/brak	17/20 (85%)	24/28 (86%)	53/65 (82%)	29/34 (85%)	13/16 (81%)
1+ łagodna	3/20 (15%)	3/28 (11%)	6/65 (9%)	3/34 (9%)	3/16 (19%)
2+ umiarkowana	0/20 (0%)	0/28 (0%)	3/65 (5%)	2/34 (6%)	0/16 (0%)
3+ umiarkowana/ciężka	0/20 (0%)	0/28 (0%)	1/65 (2%)	0/34 (0%)	0/16 (0%)
4+ ciężka	0/20 (0%)	0/28 (0%)	0/65 (0%)	0/34 (0%)	0/16 (0%)
Niedostępne	0/20 (0%)	1/28 (4%)	2/65 (3%)	0/34 (0%)	0/16 (0%)

Uwagi:

1. Oceny hemodynamiczne wykonane były z zastosowaniem przezklatkowego badania echokardiograficznego (TTE) oraz – w niektórych przypadkach – przezprzełykowego badania echokardiograficznego (TEE).
2. Średni gradient wyrażony w mmHg
3. EOA: Efektywne pole ujścia, cm^2
4. Fala zwrotna = Nieznaczna/brak, 0; łagodna, 1+; umiarkowana, 2+; umiarkowana/ciężka, 3+; ciężka, 4+

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Symbol Legend • Légende des symboles • Legenda Symboli

	English	Français	Polski
REF	Catalogue Number	Numéro de référence	Numer Katalogowy
⚠	Caution	Attention	Przestroga
	Consult instructions for use	Consulter le mode d'emploi	Zapoznać się z instrukcją użycia
2	Single Use	À usage unique	Do jednorazowego użytku
#	Quantity	Quantité	Ilość
	Use By	Utiliser avant	Zużyć Do
SN	Serial Number	Numéro de série	Numer Serii
	Manufacturer	Fabricant	Producent
SZ	Size	Taille	Rozmiar

	English	Français	Polski
STERILE EO	Ethylene Oxide Sterilized	Stérilisé à l'oxyde d'éthylène	Wysterylizowano Przy Użyciu Tlenku Etylenu
	Do not use if package is opened or damaged.	Ne pas utiliser si l'emballage est ouvert ou endommagé.	Nie używać, jeśli opakowanie jest otwarte lub uszkodzone.
EC REP	European Authorized Representative	Mandataire européen	Autoryzowany przedstawiciel w Europie
STERILE	Contents sterile and nonpyrogenic if package is unopened or undamaged.	Contenu stérile et apyrogène si le conditionnement n'est ni ouvert ni endommagé.	Zawartość sterylna i niepirogenna, o ile opakowanie nie zostało otwarte ani uszkodzone.
25 °C 10 °C	Do not freeze - Store between 10 °C and 25 °C	Ne pas congeler - Conserver entre 10 °C et 25 °C	Nie zamrażać - Przechowywać w temperaturze od 10 °C do 25 °C

Note: Not all symbols may be included in the labeling of this product. • **Remarque :** il est possible que certains symboles n'apparaissent pas sur les étiquettes de ce produit. • **Uwaga:** Nie wszystkie symbole muszą być użyte na etykietach niniejszego produktu.

GLX3SL5x7.1

EC REP

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Edwards Irvine, CA 92614	Title: IFU, 11000M, IDE, E, F, P		
	Part Number: 199663003 Rev.: A	Page 61 of 61	ECR: 118879
	Graphic Artist: Glenn Getler		Date: 3/6/14

First Proofer: Lenore Dunn	Date: 3/7/14	Second Proofer: See below	Date:
Full Proof [ ] Proofed Against Redline [ ] Docuproof [X]		Full Proof [X] Proofed Against Redline [X] Docuproof [ ]	

First Proofer: n/a	Date: n/a	Second Proofer: Theresa Menchaca	Date: 3/7/14
Pages: n/a		Pages: 1 - 19, 49 - 61	

First Proofer: n/a	Date: n/a	Second Proofer: Lee Vibber	Date: 3/7/14
Pages: n/a		Pages: 20 - 48	

NOTE
1. ALL ART PRINTS 100% BLACK UNLESS OTHERWISE NOTED.
2. PROOF IS 100% OF ACTUAL PRINTED SIZE.

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ATTACHMENT C – INFORMED CONSENT FORM TEMPLATE

SAMPLE INFORMED CONSENT – Model 11000A

Subject Information

CLINICAL TRIAL # 2012-02 (AORTIC CONSENT FORM, CONTINUED FOLLOW-UP)

*Prospe**C**tive, n**O**n-rando**M**ized, **M**ultic**EN**ter **C**linical evaluation of the **E**dwards Pericardial Aortic & Mitral Bioprostheses (Models 11000A and 11000M) with a new tissue treatment platform (COMMENCE TRIAL)*

You are invited to take part in a clinical research trial. This information sheet tells you why the research is being done and what it would involve for you if you chose to take part. Please read the following information carefully and feel free to discuss this with your family or your doctor. If you are unclear about anything or would like more information, please contact, <*Name*> on <*Tel. number*>. Give yourself time to decide whether or not you wish to take part. Your participation in this research trial is voluntary. If you decide to participate, we will ask you to sign this document in order to state your agreement. This trial is given a favorable opinion by the Institutional Review Board and by the US Food and Drug Administration (FDA). It will be conducted according to the regulations governing clinical research. A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Introduction

The heart contains four (4) valves, which allow the blood to flow in the correct direction. When a valve does not work properly, the heart has to work harder in order to pump the required amount of blood to the body. This may cause symptoms that depend on the valve that is damaged and the amount of the damage. If the damage is serious, surgery to remove and replace the damaged valve with a new valve is recommended.

What is the purpose of this trial?

The objective of this trial is to confirm that modifications to tissue processing, valve sterilization, and packaging of the FDA-approved (P860057/S042) Carpentier-Edwards PERIMOUNT Magna Ease Pericardial Bioprosthesis, Model 3300TFX (designated as the Edwards Pericardial Aortic Bioprosthesis, Model 11000A) do not raise any new questions of safety and effectiveness in subjects who require replacement of their native or prosthetic aortic valve. The only differences between the Model 3300TFX and the Model 11000A are modifications in tissue processing, valve sterilization, and packaging. Data collected in this clinical investigation was submitted to the FDA, and the Model 11000A valve is now approved to sell in the United States. In order to obtain sufficient long-term data on the valve, up to 250 Subjects at up to 10 hospitals that consent to extended follow-up will continue to be followed in this trial for up to 10 years (an additional 5 years from original study design).

Why am I asked to participate to this research trial?

You are being asked to continue to participate in this trial because continued follow up beyond the original 5 year duration is a request by the FDA so that Edwards may obtain long term

performance data on the valve that you received. This new aortic valve was developed to treat subjects having aortic valve disease like you.

Trial design

Up to 700 aortic valve replacement subjects and up to 175 mitral valve replacement subjects in up to 40 hospitals located throughout the United States, Canada, Europe and Asia Pacific will be enrolled in this trial. Your participation in this trial will not change your planned surgical treatment as all enrolled subjects will receive the Model 11000A valve, unless contraindicated by the trial doctor. The entire length of the trial is expected to last up to 10.5 years. Your participation will last for 10 years. You will be asked to return to the hospital where the surgery was done and be checked by the trial doctor or his/her colleagues. You will be assessed at discharge, 1 month, at 3 months, 12 months, and annually thereafter for 10 years from the time of implant of the Model 11000A valve into your heart. Please note the 1 month visit will be conducted by phone.

Description of the Edwards Pericardial Aortic Bioprosthesis, Model 11000A

The Edwards Pericardial Aortic Bioprosthesis, Model 11000A is an FDA-approved device. The Model 11000A valve is an FDA-approved Carpentier-Edwards PERIMOUNT Magna Ease 3300TFX valve, with modifications in tissue processing, valve sterilization, and packaging.

The Magna Ease valve consists of three tissue leaflets made of bovine (cow) pericardium (heart tissue). These leaflets have been treated with a new Edwards tissue process, built on the FDA-approved Edwards ThermaFix process to stabilize and preserve tissue. This process also allows the Model 11000A to be stored in non-liquid packaging and to not require rinsing prior to implant.

How was the valve under investigation tested?

The valve was tested, on animals and in bench-top laboratory testing, in conformity with the U.S. Regulations. The valve also has been implanted in 133 patients in Europe. Preliminary results of these tests to date have shown that the valve is suitable for implant in humans.

The technique used for implanting the valve is the same as your doctor uses with other biological heart valves. Each of the trial doctors involved in this clinical trial is properly trained on how to implant the Model 11000A valve.

The Model 11000A valve is being tested in ongoing clinical trials inside and outside the United States.

What will happen to me if I take part?

If you agree to participate in this trial, you will be treated like any other subject having a similar operation and you also will have some more tests (described below) to collect more information about the valve and the surgery.

The decision about participating in this trial is entirely yours. Please make sure that all your questions are addressed before you make a decision. If you consent to participate, we will ask you to sign and date this informed consent form. A copy of this form will be given to you.

The trial doctor will then ask you questions and will run tests and procedures to see if you qualify for trial participation. These tests and procedures include:

- Your blood pressure, heart rate, height, and weight will be measured (physical exam)
- Your medical history and your current medications will be reviewed
- Your blood will be collected for laboratory testing. The blood draw will consist of a needle being stuck into a vein in your arm (or other area where a vein can be accessed). Approximately two tablespoons (30 mL) of blood will be drawn at this visit for routine tests including a complete blood count, plasma free hemoglobin, or haptoglobin or serum LDH, coagulation profile, and serum creatinine to test for kidney function. Any remaining blood sample will be discarded according to hospital regulations.
- An electrocardiogram (a test using a machine that records the electrical activity of your heart. The recording is done by putting self adhesive discs on your chest)
- An echocardiogram (a test using a machine that creates sound waves creating pictures of inside your heart. A small probe is put on the outside of your chest)
- The severity of your health will be graded using a standard scale by the New York Heart Association (NYHA) based on your ability to do physical activities
- You will complete a questionnaire to assess your quality of life
- If you are a woman of child-bearing age (and are not sterile) a small amount of blood or urine will be obtained to check for pregnancy

If the results of the tests and examinations do not meet the trial requirements and your doctor assesses that you are not qualified to participate in the trial, you will be excluded from the trial and the trial doctor will discuss with you an alternative treatment for your disease. No further commitments related to this trial will be requested from you.

If, as a result of the above mentioned tests and examinations, your doctor assesses that you are qualified to participate in the trial, you will be scheduled for surgery. Upon your approval, your personal physician will be informed of your participation in the clinical trial.

Similar to other aortic valve replacement operations, this surgical procedure is performed under general anesthesia. The cardiac surgeon reaches the heart by making a cut in the chest and opening the sternum [breast bone]. The beating of the heart is stopped and the blood circulation will continue using a “heart-lung” machine.

If during surgery your trial doctor finds a reason not to implant the Model 11000A valve, you will receive an FDA-approved aortic valve. You will not have any further commitments related to this trial.

If your trial doctor determines that there are no contraindications, you will receive the Model 11000A valve and you will be considered enrolled in the trial.

During your surgery after the Model 11000A valve is implanted, a small tube used as a probe for a transesophageal echocardiogram (TEE) will be entered through your mouth and advanced down to the area of the heart. The doctor will use this echocardiogram to take pictures of your heart. This is part of every surgery to replace a heart valve.

If the Model 11000A valve is replaced with another FDA-approved aortic valve at any time after enrollment, you will be followed for 30 days or until any symptoms or side effects you may

experience have resolved. Your investigational valve may be removed or explanted and sent to the Sponsor or an independent lab for further analysis.

After your surgery and before you go home, you will have some more tests and examinations as described below:

- Your blood pressure, heart rate and weight will be measured (physical exam)
- Your current medications will be recorded
- Blood tests (including a complete blood count, plasma free hemoglobin or haptoglobin or serum LDH and coagulation profile)
- An electrocardiogram (once right after your procedure, and once before you go home)
- An echocardiogram will be obtained to see that the newly implanted Model 11000A valve sits well in its position and that it works well
- You will be asked if you have experienced any unusual symptoms or side effects since the procedure – any finding will be recorded in order to control your health status

At 1 month after your surgery, you will be called and asked to provide information about your health status:

- Your current medications will be recorded
- Your health condition will be graded based on your ability to perform physical activities (NYHA class)
- You will be asked if you have experienced any unusual symptoms or side effects since your last assessment
- An appointment will be scheduled for you to return to the trial center approximately at 3 months from your procedure date

During your 3 month and subsequent annual follow-up visits, you will be asked to provide information about your health status and you will undergo the following procedures:

- Your blood pressure, heart rate and weight will be measured (physical exam)
- Your current medications will be recorded
- Blood tests (including a complete blood count, plasma free hemoglobin or haptoglobin or serum LDH, and coagulation profile)
- An electrocardiogram
- An echocardiogram
- Your health condition will be graded based on your ability to perform physical activities (NYHA class)
- You will complete a questionnaire that will help your doctor to assess your quality of life (only at 12 month follow-up)
- You will be asked if you have experienced any unusual symptoms or side effects since your last assessment

Participant responsibilities

If you decide to participate in this research trial, you will have to follow the instructions given by your trial doctor and his colleagues and return to the hospital for all the follow-up visits until the tenth follow up year. Completing all trial visits is important to make sure that the trial results are complete and accurate. If you wish to stop participating in the trial or if you find you have not followed instructions listed above, it is important that you notify the trial doctor or research staff.

Your participation in this research trial is **entirely voluntary** and it is your right to refuse to participate or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. You are free to withdraw from the trial at any time without giving any reason, even if you have confirmed in writing that you want to take part. Your decision to withdraw will not have any adverse effect whatsoever on your further treatment in our hospital.

Giving false, incomplete, or misleading information about your medical history, including past and present use of medications, could have a very serious effect on your health. It is very important that you give a true and complete medical history.

What are the possible benefits of taking part?

There are no guaranteed benefits from participation in this clinical investigation.

Potential benefits resulting from this clinical trial include:

- improvement of aortic valve function
- acute relief of symptoms related to aortic stenosis
- improvement in morbidity and mortality compared to similar/conventional devices

In addition, information gained from the conduct of this trial may be of benefit to other people with the same medical condition in the future. The long-term results of using the investigational valve are not known at the present time.

Alternative treatments include palliative medical therapy, aortic balloon valvuloplasty (opening the narrowed aortic valve with a balloon catheter) and surgical replacement of the aortic valve with another brand of prosthesis.

What are the possible risks/inconveniences of taking part?

You must understand that the treatment of choice for your condition is a heart valve replacement and that alternative valves are available.

As with all prosthetic heart valves, there is a possibility that serious complications, sometimes leading to death, could develop that were not anticipated. In addition, complications and inconveniences due to individual subject reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin may occur, necessitating reoperation and replacement of the prosthetic device. These risks will be explained to you by your trial doctor. Unforeseeable risks may also occur. Should any side effects occur, they will be fully assessed and you will be monitored closely.

You may experience events and/or outcomes that may include, but are not necessarily limited to, the following:

Known/potential risks associated with the use of stented bioprosthetic heart valves include but are not limited to:

- Angina *(chest pain or other pain from the heart)*
- Bleeding diatheses/coagulopathy related to anticoagulant therapy *(increased susceptibility to bleeding)*
- Cardiac arrhythmias *(change in or blockage of the heartbeat rhythm)*
- Cardiac failure
- Coronary ostial blockage *(blockage of opening of coronary artery)*
- Endocarditis *(infection of the valve)*
- Hemolysis/Hemolytic anemia *(breaking open of red blood cells with release of hemoglobin)*
- Hemorrhage *(bleeding)*
- Immunological response
- Leaflet entrapment (*impingement*)
- Myocardial infarction *(heart attack)*
- Nonstructural valve dysfunction
- Malfunctions of valve due to distortion at implant, fracture of wireform, physical and or chemical deterioration of valve components
- Paravalvular/Perivalvular leak *(blood leaking around the valve when it is closed)*
- Patient prosthetic mismatch (PPM) *(inappropriate sizing)*
- Regurgitation/insufficiency *(blood leaking through the valve when it is closed)*
- Stenosis *(narrowing of the valve)*
- Thromboembolism/stroke *(blood clot breaking off from the valve and causing blockage in the circulation downstream)*
- Tissue deterioration including infection, calcification, thickening, perforation, degeneration, suture abrasion, instrument trauma, and or leaflet detachment
- Transient ischemic attack (TIA) *(mini-stroke)*
- Valve pannus *(excessive tissues growth around the valve)*
- Valve thrombosis *(blood clot attachment to the valve)*

Potential risks associated with aortic valve replacement surgery include but are not limited to:

- Allergic reaction
- Annular dissection *(tear in the tissue around valve opening)*
- Aortic/arterial dissection *(tear in the artery)*
- Bleeding, anticoagulant related (related to blood thinners)
- Bleeding, procedural/post-procedural *(during or after surgery)*
- Cardiac arrest *(heart stops beating)*
- Cardiogenic shock *(not enough blood being pumped by the heart)*
- Disseminated intravascular coagulation (DIC) *(the blood clots too much)*
- Esophageal rupture *(tear or hole in the tube that connects the mouth to the stomach)*

- Heart failure
- Hematoma *(localized collection of blood)*
- Heparin induced thrombocytopenia (HITs) *(low platelet count in blood due to medication)*
- Hypertension/Hypotension *(blood pressure that is too low or too high)*
- Hypoxemia *(lack of oxygen)*
- Infection, local or wound
- Infection, systemic (body-wide, called septicemia)
- Myocardial Infarction *(heart attack)*
- Multi-system organ failure (MOF) *(example liver and or kidneys stop working)*
- Pericardial effusion *(fluid around the heart)*
- Pericardial tamponade *(a large amount of fluid around the heart such that is interferes with its normal performance)*
- Pleural effusion *(fluid around the lungs)*
- Pulmonary edema *(fluid in the lungs)*
- Pneumonia *(infection of the lungs)*
- Renal dysfunction *(kidney function worsening)*
- Respiratory failure *(lung failure where the level of oxygen in the blood becomes dangerously low)*
- Thromboembolism *(blood clot)*
  - Venous, peripheral or central *(blood clot in vein)*
  - Arterial, peripheral or central *(blood clot in artery)*
  - Pulmonary, thrombus *(blood clot in lung)*

These complications may manifest clinically as symptoms including but not limited to abnormal heart murmur, exercise intolerance, shortness of breath, anemia, and/or fever.

It is possible that these complications could lead to:

- Reoperation
- Explant (removal of the valve)
- Permanent disability
- Death

Risks associated with the Model 11000A are anticipated to be the same as listed above for other aortic bioprosthetic valves and valve replacement surgery.

You may require anti-coagulant therapy (a substance that prevents clotting of the blood) as a result of having your aortic valve replaced with the Model 11000A valve. You may require long-term anti-platelet therapy (aspirin, unless there is a reason you should not take it) even if long-term anti-coagulant therapy is not required.

Post procedural anti-coagulant and anti-platelet medications include the risk of causing severe bleeding and heavy blood loss. Because of this risk, anyone taking these drugs must take care to avoid injuries. Any falls, blows to the body or head, or other injuries should be reported to a physician, as internal bleeding may occur without any obvious symptoms. Post procedural anti-coagulation and associated risks are no different with the investigational valve than with valves already approved by the FDA.

Risks from taking a blood sample

You will have routine blood samples taken from a vein in your arm by a needle stick. Risks associated with drawing blood from your arm include slight discomfort and/or bruising. Infection, bleeding, clotting, or fainting also are possible, although unlikely. The number of times that you will have a blood sample drawn for this trial is maximal 8 times over approximately 5 years. At maximum, two tablespoons (30 mL) of blood will be taken at a single visit.

Risks from an electrocardiogram

In rare circumstances, a rash or irritation at the location of the electrocardiogram electrode placement can occur due to the adhesive. If this should occur, it will be assessed and treated using clinical standards of care with appropriate medication(s) and/or compresses.

Risks from an echocardiogram

A lubricant (gel) is used on the skin to improve picture quality and this may feel cold. There are no known risks associated with receiving a transthoracic echocardiogram.

Risks from an transesophageal echocardiography (TEE)

The few risks of TEE involve passing the probe from your mouth down into your throat and esophagus. You may have a sore throat for a day or two. In very rare cases, TEE causes the esophagus to bleed.

If I decide against participating in the clinical trial what other options do I have?

If you decide not to participate in this trial, you can discuss with your doctor which options of heart valve replacement best suit your requirements. There are a number of brands of bioprosthetic valves available. Alternatives available to you may include continuation of your current heart medications and treatments without having surgery to replace your aortic valve. It is important that you discuss these other options with your doctor. This does not in any way affect your further clinical care.

What if something goes wrong?

Your doctor and Edwards Lifesciences LLC will take all appropriate efforts to prevent any injury or illness which may occur as a result of your participation in this trial. If you suffer any injury or illness as a direct result of participating in this trial, you will receive medical care and treatment at this hospital. Call your trial doctor immediately. Signing this consent does not affect any legal rights you have.

Will my taking part in this trial be kept confidential?

The records of this trial will be kept confidential. This section explains how your medical records might be used and disclosed if you agree to participate in this trial.

All physicians involved in the trial follow a strict clinical protocol. You have the right to determine who has access to your health records. Records collected in this trial includes your medical history, the results of physical exams, lab tests and other diagnostic procedures as described

above in this consent form, as well as basic demographic information and data related to your trial treatment.

By signing this form:

- You allow the research staff and/or the trial doctor to use your medical records for the trial and to disclose your health information to the Sponsor, Edwards Lifesciences LLC, or to the sponsor's representatives, in order to review the results of the trial and to monitor the safety of participants.
- You allow the trial doctor and/or sponsor to publish the results of the trial or discuss the results at conferences. If this is done, no information will be included that would reveal your identity.

The information sent by the trial doctor and/or research staff to the Sponsor will not include your name, address, or other identifiers. Instead, the trial doctor will assign a coded number to the records that are provided to the Sponsor. However, your entire medical record may be reviewed at the trial doctor's office and/or hospital by the Sponsor and/or Sponsor representatives, by regulatory/government agencies including the Food and Drug Administration (FDA) and the independent Institutional Review Board (IRB - a committee formally selected to approve, review and monitor research involving human subjects), and/or other regulatory agencies in other countries. The purpose of these reviews is to assure the safety and well-being of trial participants and the quality of the clinical trial.

The trial doctor and/or research staff will make every effort to protect the privacy of your information. However, absolute confidentiality cannot be guaranteed because of the need to disclose information as described above.

This authorization does not have an expiration date. If you do not cancel this authorization then it will remain in effect indefinitely.

You can cancel this authorization at any time by giving a written notice to the trial doctor. If you cancel this authorization, then you no longer will be able to participate in the trial, and the information that was collected prior to canceling the authorization may still be used and disclosed to the above-mentioned parties. You will receive a signed copy of this consent for your records.

All data collected within the scope of the trial may be forwarded to other persons or institutions not authorized for direct data inspection in an anonymized form only.

Participation and Withdrawal

You have the right to choose not to be in this trial or to stop being a part of this trial at any time without any consequences. This means that there will be no penalty or loss of medical benefits to which you are entitled.

If you choose to stop being a part of this trial, you must first notify the trial doctor immediately so that a plan can be provided for your continued medical care. At the time you stop taking part in the trial, you will be asked to return for a final safety evaluation that will include gathering information about your current medical condition and conducting any required procedures. For your own safety, you should go through the trial exit procedures any time you leave the trial and make arrangements for your continued medical care.

It is possible that your participation in this trial may be stopped at any time without asking you. This might happen if you do not follow the instructions given by the trial doctor or if the trial

doctor believes it is in your best interest. The trial also may be stopped for administrative, medical, or other reasons as determined by the trial doctor, the Sponsor, or regulatory authorities. Any significant new findings developed during the course of this research that might affect your willingness to participate in the trial will be provided to you and the trial doctor.

While participating in this trial, you should not take part in any other clinical trial. This is to protect you from possible injury that may arise.

Who is organizing and funding the research?

This trial/research is organized by Edwards Lifesciences LLC, the Sponsor and the company that makes the Model 11000A valve. The clinical research staff will not be paid to include you in this trial but the hospital will be reimbursed for the costs incurred in conducting this research.

Costs and Compensation

You will be billed for all charges normally associated with heart valve replacement (including trial-related visits) – only those required procedures outside of the routine standard of care will be paid for by the sponsor. There will be no financial compensation for your participation in this clinical trial.

You will be reimbursed for the travel expenses you have in order to return to the hospital for the follow-up visits required during the trial. You will still be responsible for the cost of your usual ongoing medical care, including procedures and/or non-trial drugs that are not required by this clinical research trial. If you have any questions, please ask the trial doctor, or a member of the research staff.

You understand that all forms of medical diagnosis and treatment, whether routine or trial-related, involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this research trial. You understand that the Sponsor or the hospital cannot assume liability for injury caused by the use of this particular valve or any other valve. In the event physical injury occurs as a result of participating in this research trial, the necessary facilities, emergency treatment and professional medical services will be available to you, just as they are to anyone. In the event of an unexpected injury directly related to the investigational device or the procedures described in the Clinical Research Protocol, the Sponsor will reimburse the hospital for the cost of treatment for any such injury, under the following conditions:

- The costs of treatment are not paid for by your medical or hospital insurance or coverage; and
- The injury is not due to negligence of the Investigator or the hospital;
- The Investigator and the hospital have followed the Clinical Protocol requirements; and
- You have followed the instructions of the Investigator

You further understand that you do not waive any liability rights for personal injury by signing this form.

Contact details for further information

If you require any further information before or during the trial, or if you have any questions after you have read this Subject Information Sheet/ Informed Consent, please contact the trial doctor responsible for you:

Trial Doctor: _____ Phone: _____

Further information

You consent to participate in a research trial and your data will be used in the statistical analysis of that clinical trial. It is understood that your personal identifiable data continues to be subject to data protection and shall not be disclosed to any third parties. Participation in this clinical trial is voluntary, and you can discontinue participation at any time without giving reasons, and without penalty. The Principal Investigator or the Sponsor also may decide on your premature discontinuation in this trial.

Signature of subject or his/her legal representative

I have received written information about the clinical trial or the information was read out to me and I had sufficient time to read this through and think about it. I also was orally informed in detail by _____ (name of clinical investigator) about the nature, significance and scope of the clinical trial; in particular about the objectives, conduct, benefit, risk, and insurance coverage including the associated obligations. All my questions were answered in an understandable way. I do not have any further questions right now. I know that I can ask questions at any time, including during and after the clinical trial.

- I declare my voluntary consent to the clinical trial. I am aware that I can refuse to participate or withdraw my consent at any time without incurring any penalties or disadvantages.
- I agree that my medical data may be recorded in the context of this clinical trial. I agree that the medical data may be forwarded in anonymous form to authorized specialists for data processing and scientific evaluation and to the competent authorities for review.
- At the same time, I agree that my health data may be recorded in the context of this clinical trial and representatives of the Sponsor or the regulatory agencies may inspect my data for review purposes.
- Finally, I agree to scientific publication of the research results in compliance with provisions of data protection legislation.

_____ I agree / _____ I do not agree that my primary care physician may be informed about my participation in this trial.

Print name of trial participant	Date	Time[1]

Signature of trial participant

Print name of legal representative (if required)	Date	Time

Signature of legal representative (if required)

Signature of Person Obtaining Consent

I have explained the clinical trial to the subject or his/her legal representative and answered all his/her questions. I have the impression that he/she understands the information contained in this document and gives his/her consent to participate on his/her own free will. The subject was given a copy of the signed consent form.

Name of Person Obtaining Consent (printed)	Date	Time

Signature of Person Obtaining Consent	Clinic

[1] Required only if consent is taken on the same day as the trial procedure

SAMPLE INFORMED CONSENT- Model 11000M

Subject Information

CLINICAL TRIAL # 2012-02 (MITRAL CONSENT FORM, CONTINUED FOLLOW-UP)

*Prospe**C**tive, n**O**n-rando**M**ized, **M**ultic**EN**ter **C**linical evaluation of the **E**dwards Pericardial Aortic & Mitral Bioprostheses (Models 11000A & 11000M) with a new tissue treatment platform (COMMENCE TRIAL)*

You are invited to take part in a clinical research trial. This information sheet tells you why the research is being done and what it would involve for you if you chose to take part. Please read the following information carefully and feel free to discuss this with your family or your doctor. If you are unclear about anything or would like more information, please contact, <*Name*> on <*Tel. number*>. Give yourself time to decide whether or not you wish to take part. Your participation in this research trial is voluntary. If you decide to participate, we will ask you to sign this document in order to state your agreement. This trial is given a favorable opinion by the Institutional Review Board and by the US Food and Drug Administration (FDA). It will be conducted according to the regulations governing clinical research. A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Introduction

The heart contains four (4) valves, which allow the blood to flow in the correct direction. When a valve does not work properly, the heart has to work harder in order to pump the required amount of blood to the body. This may cause symptoms that depend on the valve that is damaged and the amount of the damage. If the damage is serious, surgery to remove and replace the damaged valve with a new valve is recommended.

What is the purpose of this trial?

The objective of this trial is to confirm that modifications to tissue processing, valve sterilization, and packaging of the FDA-approved (P860057/S068) Carpentier-Edwards PERIMOUNT Magna Mitral Ease Pericardial Bioprosthesis, Model 7300TFX, which will be designated as the Edwards Pericardial Mitral Bioprosthesis Model 11000M, do not raise any new questions of safety and effectiveness in subjects who require replacement of their native or prosthetic mitral valve. The only differences between the Model 7300TFX and the Model 11000M are modifications in tissue processing, valve sterilization, and packaging. Data collected in this clinical investigation was submitted to the FDA, and the Model 11000M valve is now approved to sell in the United States. In order to obtain sufficient long-term data on the valve, up to 25 Subjects at select hospitals that consent to extended follow-up will continue to be followed in this trial for up to 10 years (an additional 5 years from original study design).

Why am I asked to participate to this research trial?

You are being asked to continue to participate in this trial as requested by the FDA so that Edwards may obtain long term safety and performance data on the valve that you received. This new mitral valve was developed to treat subjects having mitral valve disease like you.

Trial design

Up to 700 aortic valve replacement subjects and up to 175 mitral valve replacement subjects in up to 40 hospitals located throughout the United States, Canada, Europe and Asia Pacific will be enrolled in this trial. Your participation in this trial will not change your planned surgical treatment as all enrolled subjects will receive the Model 11000M valve, unless contraindicated by the trial doctor. The entire length of the trial is expected to last up to 10.5 years. Your participation will last for 10 years. You will be asked to return to the hospital where the surgery was done and be checked by the trial doctor or his/her colleagues. You will be assessed at discharge, 1 month, 3 months, 12 months, and annually thereafter for 10 years from the time of implant of the Model 11000M valve into your heart. Please note the 1 month visit will be conducted by phone.

Description of the Edwards Pericardial Mitral Bioprosthesis, Model 11000M

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M is an FDA-approved device. The Model 11000M valve is an FDA-approved Carpentier-Edwards PERIMOUNT Magna Mitral Ease 7300TFX valve, with modifications in tissue processing, valve sterilization, and packaging.

The Magna Mitral Ease valve consists of three tissue leaflets made of bovine (cow) pericardium (heart tissue). These leaflets have been treated with a new Edwards tissue process, built on the FDA-approved Edwards ThermaFix process to stabilize and preserve tissue. This process also allows the Model 11000M to be stored in non-liquid packaging and to not require rinsing prior to implant.

How was the valve under investigation tested?

The valve was tested on animals and in bench-top laboratory testing, in conformity with the U.S. Regulations. The results of these tests to date have shown that the valve is suitable for implant in humans.

The technique used for implanting the valve is the same as your doctor uses with other biological heart valves. Each of the trial doctors involved in this clinical trial is properly trained on how to implant the Model 11000M valve.

The Model 11000M valve is being tested in ongoing clinical trials.

What will happen to me if I take part?

If you agree to participate in this trial, you will be treated like any other subject having a similar operation and you also will have some more tests (described below) to collect more information about the valve and the surgery.

The decision about participating in this trial is entirely yours. Please make sure that all your questions are addressed before you make a decision. If you consent to participate, we will ask you to sign and date this informed consent form. A copy of this form will be given to you.

The trial doctor will then ask you questions and will run tests and procedures to see if you qualify for trial participation. These tests and procedures include:

- Your blood pressure, heart rate, height, and weight will be measured (physical exam)
- Your medical history and your current medications will be reviewed
- Your blood will be collected for laboratory testing. The blood draw will consist of a needle being stuck into a vein in your arm (or other area where a vein can be accessed). Approximately two tablespoons (30 mL) of blood will be drawn at this visit for routine tests including a complete blood count, plasma free hemoglobin or haptoglobin or serum LDH coagulation profile, and serum creatinine to test for kidney function. Any remaining blood sample will be discarded according to hospital regulations.
- An electrocardiogram (a test using a machine that records the electrical activity of your heart. The recording is done by putting self-adhesive discs on your chest)
- An echocardiogram (a test using a machine that creates sound waves creating pictures of inside your heart. A small probe is put on the outside of your chest)
- The severity of your health will be graded using a standard scale by the New York Heart Association (NYHA) based on your ability to do physical activities
- You will complete a questionnaire to assess your quality of life
- If you are a woman of child-bearing age (and are not sterile) a small amount of blood or urine will be obtained to check for pregnancy

If the results of the tests and examinations do not meet the trial requirements and your doctor assesses that you are not qualified to participate in the trial, you will be excluded from the trial and the trial doctor will discuss with you an alternative treatment for your disease. No further commitments related to this trial will be requested from you.

If, as a result of the above mentioned tests and examinations, your doctor assesses that you are qualified to participate in the trial, you will be scheduled for surgery. Upon your approval, your personal physician will be informed of your participation in the clinical trial.

Similar to other mitral valve replacement operations, this surgical procedure is performed under general anesthesia. The beating of the heart is stopped and the blood circulation will continue using a “heart-lung” machine.

If during surgery your trial doctor finds a reason not to implant the Model 11000M valve, you will receive an FDA-approved mitral valve. You will not have any further commitments related to this trial.

If your trial doctor determines that there are no contraindications, you will receive the Model 11000M valve and you will be considered enrolled in the trial.

During your surgery after the Model 11000M valve is implanted, a small tube used as a probe for a transesophageal echocardiogram (TEE) will be entered through your mouth and advanced down to the area of the heart. The doctor will use this echocardiogram to take pictures of your heart. This is part of every surgery to replace a heart valve.

If the Model 11000M valve is replaced with another FDA-approved mitral valve at any time after enrollment, you will be followed for 30 days or until any symptoms or side effects that you may experience have resolved. Your investigational valve may be removed or explanted and sent to the Sponsor or an independent lab for further analysis.

After your surgery and before you go home, you will have some more tests and examinations as described below:

- Your blood pressure, heart rate and weight will be measured (physical exam)
- Your current medications will be recorded
- Blood tests (including a complete blood count, plasma free hemoglobin or haptoglobin or serum LDH and coagulation profile)
- An electrocardiogram (once right after your procedure, and once before you go home)
- An echocardiogram will be obtained to see that the newly implanted Model 11000M valve sits well in its position and that it works well
- You will be asked if you have experienced any unusual symptoms or side effects since the procedure – any finding will be recorded in order to control your health status

At 1 month after your surgery, you will be called and asked to provide information about your health status:

- Your current medications will be recorded
- Your health condition will be graded based on your ability to perform physical activities (NYHA class)
- You will be asked if you have experienced any unusual symptoms or side effects since your last assessment
- An appointment will be scheduled for you to return to the trial center approximately at 3 months from your procedure date

During your 3 month and subsequent annual follow-up visits, you will be asked to provide information about your health status and you will undergo the following procedures:

- Your blood pressure, heart rate and weight will be measured (physical exam)
- Your current medications will be recorded
- Blood tests (including a complete blood count, plasma free hemoglobin or haptoglobin or serum LDH, and coagulation profile)
- An electrocardiogram
- An echocardiogram
- Your health condition will be graded based on your ability to perform physical activities (NYHA class)
- You will complete a questionnaire that will help your doctor to assess your quality of life (only at 12 month follow-up)
- You will be asked if you have experienced any unusual symptoms or side effects since your last assessment

Participant responsibilities

If you decide to participate in this research trial, you will have to follow the instructions given by your trial doctor and his colleagues and return to the hospital for all the follow-up visits until the tenth follow up year. Completing all trial visits is important to make sure that the trial results are complete and accurate. If you wish to stop participating in the trial or if you find you have not followed instructions listed above, it is important that you notify the trial doctor or research staff.

Your participation in this research trial is **entirely voluntary** and it is your right to refuse to participate or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. You are free to withdraw from the trial at any time without giving any reason, even if you have confirmed in writing that you want to take part. Your decision to withdraw will not have any adverse effect whatsoever on your further treatment in our hospital.

Giving false, incomplete, or misleading information about your medical history, including past and present use of medications, could have a very serious effect on your health. It is very important that you give a true and complete medical history.

What are the possible benefits of taking part?

There are no guaranteed benefits from participation in this clinical investigation.

Potential benefits resulting from this clinical trial include:

- improvement of mitral valve function
- acute relief of symptoms related to mitral stenosis
- improvement in morbidity and mortality compared to similar/conventional devices

In addition, information gained from the conduct of this trial may be of benefit to other people with the same medical condition in the future. The long-term results of using the investigational valve are not known at the present time.

Alternative treatments include palliative medical therapy, mitral balloon valvuloplasty (opening the narrowed mitral valve with a balloon catheter) and surgical replacement of the mitral valve with another brand of prosthesis.

What are the possible risks/inconveniences of taking part?

You must understand that the treatment of choice for your condition is a heart valve replacement and that alternative valves are available.

As with all prosthetic heart valves, there is a possibility that serious complications, sometimes leading to death, could develop that were not anticipated. In addition, complications and inconveniences due to individual subject reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin may occur, necessitating reoperation and replacement of the prosthetic device. These risks will be explained to you by your trial doctor. Unforeseeable risks may also occur. Should any side effects occur, they will be fully assessed and you will be monitored closely.

You may experience events and/or outcomes that may include, but are not necessarily limited to, the following:

Known/potential risks associated with the use of stented bioprosthetic heart valves include but are not limited to:

- Angina *(chest pain or other pain from the heart)*
- Bleeding diatheses/coagulopathy related to anticoagulant therapy *(increased susceptibility to bleeding)*
- Cardiac arrhythmias *(change in or blockage of the heartbeat rhythm)*
- Cardiac failure
- Coronary ostial blockage *(blockage of opening of coronary artery)*
- Endocarditis *(infection of the valve)*
- Hemolysis/Hemolytic anemia *(breaking open of red blood cells with release of hemoglobin)*
- Hemorrhage *(bleeding)*
- Immunological response
- Leaflet entrapment (*impingement*)
- Myocardial infarction *(heart attack)*
- Nonstructural valve dysfunction
- Malfunctions of valve due to distortion at implant, fracture of wireform, physical and or chemical deterioration of valve components
- Paravalvular/Perivalvular leak *(blood leaking around the valve when it is closed)*
- Patient prosthetic mismatch (PPM) *(inappropriate sizing)*
- Regurgitation/insufficiency *(blood leaking through the valve when it is closed)*
- Stenosis *(narrowing of the valve)*
- Thromboembolism/stroke *(blood clot breaking off from the valve and causing blockage in the circulation downstream)*
- Tissue deterioration including infection, calcification, thickening, perforation, degeneration, suture abrasion, instrument trauma, and or leaflet detachment
- Transient ischemic attack (TIA) *(mini-stroke)*
- Valve pannus *(excessive tissues growth around the valve)*
- Valve thrombosis *(blood clot attachment to the valve)*

Potential risks associated with mitral valve replacement surgery include but are not limited to:

- Allergic reaction
- Annular dissection *(tear in the tissue around valve opening)*
- Aortic/arterial dissection *(tear in the artery)*
- Bleeding, anticoagulant related (related to blood thinners)
- Bleeding, procedural/post-procedural *(during or after surgery)*
- Cardiac arrest *(heart stops beating)*

- Cardiogenic shock *(not enough blood being pumped by the heart)*
- Disseminated intravascular coagulation (DIC) *(the blood clots too much)*
- Esophageal rupture *(tear or hole in the tube that connects the mouth to the stomach)*
- Heart failure
- Hematoma *(localized collection of blood)*
- Heparin induced thrombocytopenia (HITs) *(low platelet count in blood due to medication)*
- Hypertension/Hypotension *(blood pressure that is too low or too high)*
- Hypoxemia *(lack of oxygen)*
- Infection, local or wound
- Infection, systemic (body-wide, called septicemia)
- Myocardial Infarction *(heart attack)*
- Multi-system organ failure (MOF) *(example liver and or kidneys stop working)*
- Pericardial effusion *(fluid around the heart)*
- Pericardial tamponade *(a large amount of fluid around the heart such that is interferes with its normal performance)*
- Pleural effusion *(fluid around the lungs)*
- Pulmonary edema *(fluid in the lungs)*
- Pneumonia *(infection of the lungs)*
- Renal dysfunction *(kidney function worsening)*
- Respiratory failure *(lung failure where the level of oxygen in the blood becomes dangerously low)*
- Thromboembolism *(blood clot)*
  - Venous, peripheral or central *(blood clot in vein)*
  - Arterial, peripheral or central *(blood clot in artery)*
  - Pulmonary, thrombus *(blood clot in lung)*

These complications may manifest clinically as symptoms including but not limited to abnormal heart murmur, exercise intolerance, shortness of breath, anemia, and/or fever.

It is possible that these complications could lead to:

- Reoperation
- Explant (removal of the valve)
- Permanent disability
- Death

Risks associated with the Model 11000M are anticipated to be the same as listed above for other mitral bioprosthetic valves and valve replacement surgery.

You may require anti-coagulant therapy (a substance that prevents clotting of the blood) as a result of having your mitral valve replaced with the Model 11000M valve. You may require long-term anti-platelet therapy (aspirin, unless there is a reason you should not take it) even if long-term anti-coagulant therapy is not required.

Post procedural anti-coagulant and anti-platelet medications include the risk of causing severe bleeding and heavy blood loss. Because of this risk, anyone taking these drugs must take care to avoid injuries. Any falls, blows to the body or head, or other injuries should be reported to a

physician, as internal bleeding may occur without any obvious symptoms. Post procedural anti-coagulation and associated risks are no different with the investigational valve than with valves already approved by the FDA.

Risks from taking a blood sample

You will have routine blood samples taken from a vein in your arm by a needle stick. Risks associated with drawing blood from your arm include slight discomfort and/or bruising. Infection, bleeding, clotting, or fainting also are possible, although unlikely. The number of times that you will have a blood sample drawn for this trial is maximal 8 times over approximately 5 years. At maximum, two tablespoons (30 mL) of blood will be taken at a single visit.

Risks from an electrocardiogram

In rare circumstances, a rash or irritation at the location of the electrocardiogram electrode placement can occur due to the adhesive. If this should occur, it will be assessed and treated using clinical standards of care with appropriate medication(s) and/or compresses.

Risks from an echocardiogram

A lubricant (gel) is used on the skin to improve picture quality and this may feel cold. There are no known risks associated with receiving a transthoracic echocardiogram.

Risks from an transesophageal echocardiography (TEE)

The few risks of TEE involve passing the probe from your mouth down into your throat and esophagus. You may have a sore throat for a day or two. In very rare cases, TEE causes the esophagus to bleed.

If I decide against participating in the clinical trial what other options do I have?

If you decide not to participate in this trial, you can discuss with your doctor which options of heart valve replacement best suit your requirements. There are a number of brands of bioprosthetic valves available. Alternatives available to you may include continuation of your current heart medications and treatments without having surgery to replace your mitral valve. It is important that you discuss these other options with your doctor. This does not in any way affect your further clinical care.

What if something goes wrong?

Your doctor and Edwards Lifesciences LLC will take all appropriate efforts to prevent any injury or illness which may occur as a result of your participation in this trial. If you suffer any injury or illness as a direct result of participating in this trial, you will receive medical care and treatment at this hospital. Call your trial doctor immediately. Signing this consent does not affect any legal rights you have.

Will my taking part in this trial be kept confidential?

The records of this trial will be kept confidential. This section explains how your medical records might be used and disclosed if you agree to participate in this trial.

All physicians involved in the trial follow a strict clinical protocol. You have the right to determine who has access to your health records. Records collected in this trial includes your medical

history, the results of physical exams, lab tests and other diagnostic procedures as described above in this consent form, as well as basic demographic information and data related to your trial treatment.

By signing this form:

- You allow the research staff and/or the trial doctor to use your medical records for the trial and to disclose your health information to the Sponsor, Edwards Lifesciences LLC, or to the sponsor's representatives, in order to review the results of the trial and to monitor the safety of participants.
- You allow the trial doctor and/or sponsor to publish the results of the trial or discuss the results at conferences. If this is done, no information will be included that would reveal your identity.

The information sent by the trial doctor and/or research staff to the Sponsor will not include your name, address, or other identifiers. Instead, the trial doctor will assign a coded number to the records that are provided to the Sponsor. However, your entire medical record may be reviewed at the trial doctor's office and/or hospital by the Sponsor and/or Sponsor representatives, by regulatory/government agencies including the Food and Drug Administration (FDA) and the independent Institutional Review Board (IRB - a committee formally selected to approve, review and monitor research involving human subjects), and/or other regulatory agencies in other countries. The purpose of these reviews is to assure the safety and well-being of trial participants and the quality of the clinical trial.

The trial doctor and/or research staff will make every effort to protect the privacy of your information. However, absolute confidentiality cannot be guaranteed because of the need to disclose information as described above.

This authorization does not have an expiration date. If you do not cancel this authorization then it will remain in effect indefinitely.

You can cancel this authorization at any time by giving a written notice to the trial doctor. If you cancel this authorization, then you no longer will be able to participate in the trial, and the information that was collected prior to canceling the authorization may still be used and disclosed to the above-mentioned parties. You will receive a signed copy of this consent for your records.

All data collected within the scope of the trial may be forwarded to other persons or institutions not authorized for direct data inspection in an anonymized form only.

Participation and Withdrawal

You have the right to choose not to be in this trial or to stop being a part of this trial at any time without any consequences. This means that there will be no penalty or loss of medical benefits to which you are entitled.

If you choose to stop being a part of this trial, you must first notify the trial doctor immediately so that a plan can be provided for your continued medical care. At the time you stop taking part in the trial, you will be asked to return for a final safety evaluation that will include gathering information about your current medical condition and conducting any required procedures. For your own safety, you should go through the trial exit procedures any time you leave the trial and make arrangements for your continued medical care.

It is possible that your participation in this trial may be stopped at any time without asking you. This might happen if you do not follow the instructions given by the trial doctor or if the trial doctor believes it is in your best interest. The trial also may be stopped for administrative, medical, or other reasons as determined by the trial doctor, the Sponsor, or regulatory authorities. Any significant new findings developed during the course of this research that might affect your willingness to participate in the trial will be provided to you and the trial doctor.

While participating in this trial, you should not take part in any other clinical trial. This is to protect you from possible injury that may arise.

Who is organizing and funding the research?

This trial/research is organized by Edwards Lifesciences LLC, the Sponsor and the company that makes the Model 11000M valve. The clinical research staff will not be paid to include you in this trial but the hospital will be reimbursed for the costs incurred in conducting this research.

Costs and Compensation

You will be billed for all charges normally associated with heart valve replacement (including trial-related visits) – only those required procedures outside of the routine standard of care will be paid for by the sponsor. There will be no financial compensation for your participation in this clinical trial.

You will be reimbursed for the travel expenses you have in order to return to the hospital for the follow-up visits required during the trial. You will still be responsible for the cost of your usual ongoing medical care, including procedures and/or non-trial drugs that are not required by this clinical research trial. If you have any questions, please ask the trial doctor, or a member of the research staff.

You understand that all forms of medical diagnosis and treatment, whether routine or trial-related, involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this research trial. You understand that the Sponsor or the hospital cannot assume liability for injury caused by the use of this particular valve or any other valve. In the event physical injury occurs as a result of participating in this research trial, the necessary facilities, emergency treatment and professional medical services will be available to you, just as they are to anyone. In the event of an unexpected injury directly related to the investigational device or the procedures described in the Clinical Research Protocol, the Sponsor will reimburse the hospital for the cost of treatment for any such injury, under the following conditions:

- The costs of treatment are not paid for by your medical or hospital insurance or coverage; and
- The injury is not due to negligence of the Investigator or the hospital;
- The Investigator and the hospital have followed the Clinical Protocol requirements; and
- You have followed the instructions of the Investigator

You further understand that you do not waive any liability rights for personal injury by signing this form.

Contact details for further information

If you require any further information before or during the trial, or if you have any questions after you have read this Subject Information Sheet/ Informed Consent, please contact the trial doctor responsible for you:

Trial Doctor: _____ Phone: _____

Further information

You consent to participate in a research trial and your data will be used in the statistical analysis of that clinical trial. It is understood that your personal identifiable data continues to be subject to data protection and shall not be disclosed to any third parties. Participation in this clinical trial is voluntary, and you can discontinue participation at any time without giving reasons, and without penalty. The Principal Investigator or the Sponsor also may decide on your premature discontinuation in this trial.

Signature of subject or his/her legal representative

I have received written information about the clinical trial or the information was read out to me and I had sufficient time to read this through and think about it. I also was orally informed in detail by _____ (name of clinical investigator) about the nature, significance and scope of the clinical trial; in particular about the objectives, conduct, benefit, risk, and insurance coverage including the associated obligations. All my questions were answered in an understandable way. I do not have any further questions right now. I know that I can ask questions at any time, including during and after the clinical trial.

- I declare my voluntary consent to the clinical trial. I am aware that I can refuse to participate or withdraw my consent at any time without incurring any penalties or disadvantages.
- I agree that my medical data may be recorded in the context of this clinical trial. I agree that the medical data may be forwarded in anonymous form to authorized specialists for data processing and scientific evaluation and to the competent authorities for review.
- At the same time, I agree that my health data may be recorded in the context of this clinical trial and representatives of the Sponsor or the regulatory agencies may inspect my data for review purposes.
- Finally, I agree to scientific publication of the research results in compliance with provisions of data protection legislation.

_____ I agree / _____ I do not agree that my primary care physician may be informed about my participation in this trial.

Print name of trial participant	Date	Time[1]

Signature of trial participant

Print name of legal representative (if required)	Date	Time

Signature of legal representative (if required)

Signature of Person Obtaining Consent

I have explained the clinical trial to the subject or his/her legal representative and answered all his/her questions. I have the impression that he/she understands the information contained in this document and gives his/her consent to participate on his/her own free will. The subject was given a copy of the signed consent form.

Name of Person Obtaining Consent (printed)	Date	Time

Signature of Person Obtaining Consent	Clinic

[1] Required only if consent is taken on the same day as the trial procedure

ATTACHMENT D – CASE REPORT FORMS

Subject Study ID **201202** [ ][ ][ ][ ]-[ ][ ][ ] Site# [ ][ ][ ]

Inclusion Criteria

DATE OF SCREENING [ ][ ] [ ][ ][ ] [ ][ ][ ][ ]
D D M M M Y Y Y Y

YES	NO	NAP		
☐	☐		1.	SUBJECT IS 18 YEARS OR OLDER
☐	☐		2.	SUBJECT HAS PROVIDED WRITTEN INFORMED CONSENT PRIOR TO TRIAL PROCEDURES IF YES, **DATE OF CONSENT**:_____ **TIME**:_____
☐	☐		3.	SUBJECT AGREES TO ATTEND ALL FOLLOW-UP ASSESSMENTS FOR UP TO 5 YEARS AND IS WILLING TO COMPLY WITH SPECIFIED FOLLOW-UP EVALUATIONS AT CLINICAL INVESTIGATIONAL SITES THAT ARE PARTICIPATING IN THE COMMENCE TRIAL AND/OR OBTAIN THE PROTOCOL-SPECIFIED DIAGNOSTIC TESTS AT CENTERS THAT ARE UNDER THE SAME IRB OR THE SAME HEALTHCARE SYSTEM
☐	☐		4.	SUBJECT IS DIAGNOSED WITH AORTIC OR MITRAL VALVE DISEASE REQUIRING VALVE REPLACEMENT BASED ON PRE-OPERATIVE EVALUATION
☐	☐		5.	SUBJECT IS SCHEDULED TO UNDERGO PLANNED AORTIC OR MITRAL VALVE REPLACEMENT WITH OR WITHOUT CONCOMITANT BYPASS SURGERY
☐	☐	☐	6.	SUBJECT IS SCHEDULED TO UNDERGO PLANNED AORTIC VALVE REPLACEMENT WITH OR WITHOUT RESECTION AND REPLACEMENT OF THE ASCENDING AORTA FROM THE SINOTUBULAR JUNCTION AND WITHOUT THE NEED FOR CIRCULATORY ARREST FOR HEMI ARCH OR ARCH REPLACEMENT

IF ANY RESPONSE BELOW IS "YES" THE SUBJECT IS NOT ELIGIBLE FOR THE STUDY

EXCLUSION CRITERIA

YES	NO		
☐	☐	1.	SUBJECT REQUIRES EMERGENCY SURGERY
☐	☐	2.	SUBJECT REQUIRES PLANNED MULTIPLE VALVE REPLACEMENT/REPAIR (WITH THE EXCEPTION OF MITRAL VALVE REPLACEMENT WITH TRICUSPID VALVE REPAIR)
☐	☐	3.	SUBJECT HAS PRIOR VALVE SURGERY, WHICH INCLUDED IMPLANT OF A BIOPROSTHETIC VALVE, MECHANICAL VALVE, OR ANNULOPLASTY RING THAT WILL REMAIN IN SITU
☐	☐	4.	SUBJECT REQUIRES A SURGICAL PROCEDURE OUTSIDE OF THE CARDIAC AREA (E.G. VASCULAR BYPASS)
☐	☐	5.	SUBJECT REQUIRES SURGICAL REPLACEMENT OF THE AORTIC ROOT
☐	☐	6.	SUBJECT HAS ACTIVE ENDOCARDITIS/MYOCARDITIS OR ENDOCARDITIS/MYOCARDITIS WITHIN 3 MONTHS PRIOR TO THE SCHEDULED AVR SURGERY
☐	☐	7.	SUBJECT HAS RENAL INSUFFICIENCY AS DETERMINED BY CREATININE (S-CR) ≥ 2.5 MG/DL OR END-STAGE RENAL DISEASE REQUIRING CHRONIC DIALYSIS AT SCREENING VISIT
☐	☐	8.	SUBJECT HAS AN MRI OR CT-SCAN CONFIRMED STROKE, CEREBROVASCULAR ACCIDENT (CVA), OR TRANSIENT ISCHEMIC ATTACK (TIA) WITHIN 6 MONTHS (180 DAYS) OF THE VALVE SURGERY
☐	☐	9.	SUBJECT HAS ACUTE MYOCARDIAL INFARCTION (MI) WITHIN 30 DAYS PRIOR TO THE SCHEDULED AORTIC OR MITRAL VALVE REPLACEMENT SURGERY
☐	☐	10.	SUBJECT HAS PRESENCE OF NON-CARDIAC DISEASE LIMITING LIFE EXPECTANCY TO LESS THAN 12 MONTHS
☐	☐	11.	SUBJECT IS DIAGNOSED WITH HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY (HOCM)
☐	☐	12.	SUBJECT IS DIAGNOSED WITH ABNORMAL CALCIUM METABOLISM AND HYPERPARATHYROIDISM
☐	☐	13.	SUBJECT EXHIBITS A LEFT VENTRICULAR EJECTION FRACTION ≤ 20% AS VALIDATED BY DIAGNOSTIC PROCEDURE PRIOR TO PLANNED VALVE SURGERY

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YES	NO		
☐	☐	14.	SUBJECT WITH ECHOCARDIOGRAPHIC EVIDENCE OF AN INTRA-CARDIAC MASS, THROMBUS, OR VEGETATION
☐	☐	15.	SUBJECT HAS HEMODYNAMIC OR RESPIRATORY INSTABILITY REQUIRING INOTROPIC SUPPORT, MECHANICAL CIRCULATORY SUPPORT, OR MECHANICAL VENTILATION WITHIN 30 DAYS PRIOR TO THE PROCEDURE
☐	☐	16.	SUBJECT WITH LEUKOPENIA (WBC < 3.5x 10^3/µL), ACUTE ANEMIA (HGB < 10.0 GM/L OR 6 MMOL/L), OR THROMBOCYTOPENIA (PLATELET COUNT <50 x 10^3 /µL) ACCOMPANIED BY HISTORY OF BLEEDING DIATHESIS OR COAGULOPATHY
☐	☐	17.	SUBJECT HAS A PRIOR ORGAN TRANSPLANT OR IS CURRENTLY AN ORGAN TRANSPLANT CANDIDATE
☐	☐	18.	CURRENT OR RECENT PARTICIPATION (WITHIN 6 WEEKS PRIOR TO SURGERY) IN ANOTHER DRUG OR DEVICE TRIAL
☐	☐	19.	SUBJECT WAS PREVIOUSLY IMPLANTED WITH TRIAL DEVICE (MODEL 11000A OR MODEL 11000M)
☐	☐	20.	SUBJECT IS PREGNANT (FEMALE SUBJECT OF CHILDBEARING POTENTIAL ONLY), LACTATING, OR PLANNING TO BECOME PREGNANT DURING THE DURATION OF PARTICIPATION IN TRIAL
☐	☐	21.	SUBJECT IS CURRENTLY INCARCERATED OR UNABLE TO GIVE VOLUNTARY INFORMED CONSENT
☐	☐	22.	SUBJECT HAS A DOCUMENTED HISTORY OF SUBSTANCE (DRUG OR ALCOHOL) ABUSE WITHIN THE LAST 5 YEARS
☐	☐	23.	SUBJECT REQUIRES CONCOMITANT LEFT VENTRICULAR ASSIST DEVICE (LVAD) PLACEMENT

YES	NO	
☐	☐	BASED ON ANSWERS ABOVE, IS THIS SUBJECT ELIGIBLE FOR INTRA-OPERATIVE EVALUATION? IF YES, HAS A SURGERY DATE FOR THIS SUBJECT BEEN SCHEDULED? DATE: _____
☐	☐	DID THE SUBJECT'S ELIGIBILITY FOR THE STUDY CHANGE PRIOR TO ENTERING THE OPERATING ROOM FOR THE STUDY PROCEDURE? IF YES, WHY DID THE STATUS CHANGE PRIOR TO ENTERING THE OR? ☐ ADVERSE EVENT ☐ SUBJECT WITHDREW CONSENT ☐ PHYSICIAN DISCRETION

INTRA-OPERATIVE EXCLUSION CRITERIA

YES	NO	
☐	☐	SUBJECT WAS HEMODYNAMICALLY UNSTABLE DURING THE PROCEDURE REQUIRING THE PROCEDURE TO BE ABORTED PRIOR TO IMPLANTING THE DEVICE
☐	☐	SURGEON DETERMINED TRIAL VALVE CANNOT BE IMPLANTED AFTER INTRA-OPERATIVE EVALUATION AND PRIOR TO TRIAL VALVE IMPLANT FOR ANY OTHER REASON: IF YES, WHY WAS AN IMPLANT ATTEMPT NOT MADE? ☐ SUBJECT REQUIRES A SIZE NOT AVAILABLE FOR THE TRIAL VALVE ☐ MITRAL VALVE WAS REPAIRED IF YES, WHAT IS THE VALVE ETIOLOGY? ☐ DEGENERATIVE ☐ ISCHEMIC ☐ MIXED DISEASE ☐ RHEUMATIC ☐ OTHER ☐ OTHER REASON _____
☐	☐	WAS THE SUBJECT ENROLLED IN THE STUDY?

SIGNATURE

DATE [ ][ ] D D [ ][ ][ ] M M M [ ][ ][ ][ ] Y Y Y Y

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VISIT DATE: __ __ / __ __ __ / __ __ __ __
D D M M M Y Y Y Y

1. Primary method of contact with subject:

- ☐ HOSPITAL/ CLINIC VISIT
- ☐ PHONE INTERVIEW
- ☐ IN-PATIENT ADMISSION

PHYSICAL ASSESSMENT / VITAL SIGNS:

WEIGHT: _____ ☐ kg ☐ lbs
HEART RATE: _____ bpm
SYSTOLIC BLOOD PRESSURE _____mmHg
DIASTOLIC BLOOD PRESSURE _____mmHg

CURRENT NYHA CLASSIFICATION

- ☐ CLASS I
- ☐ CLASS II
- ☐ CLASS III
- ☐ CLASS IV
- ☐ NOT DONE
- ☐ NOT APPLICABLE AT DISCHARGE

CANADIAN CARDIOVASCULAR SOCIETY (CCS) ANGINA CLASS

☐ CLASS 0 ☐ CLASS I ☐ CLASS II ☐ CLASS III ☐ CLASS IV
☐ UNKNOWN ☐ NOT APPLICABLE AT DISCHARGE

CURRENT MEDICATIONS

YES NO
☐ ☐ MEDICATION LIST WAS COLLECTED

ECHOCARDIOGRAPHY

YES NO
☐ ☐ ECHOCARDIOGRAM WAS COMPLETED

DATE OF EXAM: _____ **(DD/MMM/YYYY)**

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ELECTROCARDIOGRAM (ECG):

YES NO
☐ ☐ ECG WAS COMPLETED

DATE OF EXAM: _____ (DD/MMM/YYYY)

CARDIAC RHYTHM / CONDUCTION DISTURBANCES

YES NO

☐ ☐ IMPLANTED WITH PERMANENT PACEMAKER (IF YES, SPECIFY TYPE)
- ☐ CONTINUOUS
- ☐ INTERMITTENT (Rate responsive/ On demand)

☐ ☐ IMPLANTED WITH IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD/AICD)

☐ ☐ SINUS RHYTHM

☐ ☐ SINUS TACHYCARDIA

☐ ☐ SINUS BRADYCARDIA

☐ ☐ ATRIAL FIBRILLATION/ SUPRAVENTRICULAR TACHYCARDIA (INDICATE EPISODAL PATTERN)
- ☐ PAROXYSMAL (SELF-TERMINATING)
- ☐ PERSISTENT (NON-SELF TERMINATING)

☐ ☐ ATRIAL FLUTTER

☐ ☐ TACHYCARDIA-BRADYCARDIA SYNDROME

☐ ☐ VENTRICULAR TACHYCARDIA (IF YES, INDICATE EPISODAL PATTERN)
- ☐ NONSUSTAINED/PREMATURE VENTRICULAR COMPLEXES (PVC)
- ☐ SUSTAINED

☐ ☐ OTHER CARDIAC ARRHYTHMIA (IF YES, SPECIFY)_____

☐ ☐ AV BLOCK (IF YES, INDICATE DEGREE)
- ☐ 1ST ☐ UNKNOWN
- ☐ 2ND
- ☐ 3RD

☐ ☐ BUNDLE BRANCH BLOCK/ INTRAVENTRICULAR CONDUCTION DELAY (IF YES, INDICATE BRANCH)
- ☐ LEFT – COMPLETE ☐ RIGHT - COMPLETE
- ☐ LEFT- INCOMPLETE ☐ RIGHT- INCOMPLETE

☐ ☐ OTHER CONDUCTION DISTRUBANCE, SPECIFY:

_____

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BLOOD DATA

YES NO
☐ ☐ BLOOD LABS WERE DRAWN AT THIS VISIT

QUALITY OF LIFE SURVEY

YES NO
☐ ☐ QOL SURVEY COMPLETED?

DID ANY ADVERSE EVENTS OCCUR SINCE THE LAST FOLLOW-UP ASSESSMENT? ☐ YES ☐ NO

IF YES, COMPLETE ADVERSE EVENT FORM

Categories include:

Blood and lymphatic (including ALL bleeding complications)
Cardiovascular –Arrhythmia
Cardiovascular - Regurgitation
Cardiovascular - Stenosis
Cardiovascular - Embolic Event/Valve Thrombosis
Cardiovascular - Misc
Device Dysfunction
Gastrointestinal/Hepatic
Genitourinary/Renal
Pulmonary/Respiratory
Peripheral Vascular
Psychiatric
Muscular Skeletal/Dermatologic
Nonspecific or Unknown Body System

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DATE SIGNED | | | | | | | | | | |
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VISIT DATE: __ __ / __ __ __ / __ __ __ __
D D M M M Y Y Y Y

DATE OF BIRTH __ __ / __ __ __ / __ __ __ __ **OR YEAR** __ __ __ __ **AND AGE** __ __ __
D D M M M Y Y Y Y Y Y Y Y Y Y Y

GENDER ☐ **MALE** ☐ **FEMALE**

PREGNANCY TEST (IF FEMALE**)**

☐ **NOT PERFORMED**

☐POST-MENOPAUSAL / SURGICALLY STERILE

☐OTHER _____

☐ **PERFORMED**

☐ **POSITIVE** ☐ **NEGATIVE**

DATE TEST PERFORMED_____ (DD/MMM/YYYY)

RACE/ ETHNICITY

☐ DECLINED TO IDENTIFY

ETHNICITY

☐ HISPANIC OR LATINO

☐ NOT HISPANIC OR LATINO

RACE

☐ AMERICAN INDIAN OR ALASKA NATIVE

☐ ASIAN

☐ AFRICAN AMERICAN OR BLACK

☐ NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER

☐ WHITE

SUBJECT HEIGHT: _____☐ cm ☐ in

CURRENT LEFT VENTRICULAR EJECTION FRACTION (LVEF) _____ %

SERUM CREATININE LEVEL (mg/dL) _____

IS THIS VALUE WITHIN THE NORMAL RANGE?

☐NO

WAS THIS RESULT CLINICALLY SIGNIFICANT?

☐NO ☐YES

☐YES

_____ DATE __ __ / __ __ __ / __ __ __ __
SIGNATURE D D M M M Y Y Y Y

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Blood Draw Date: __ __ / __ __ __ / __ __ __ __
D D M M M Y Y Y Y

Blood Parameters

DONE	NOT DONE	Values	Is this value within normal ranges? Yes	Is this value within normal ranges? No	Was the result clinically significant? Yes	Was the result clinically significant? No
☐	☐	WHITE BLOOD CELLS (WBC): _____ 10^3/ µL	☐	☐	☐	☐
☐	☐	RED BLOOD CELLS (RBC): _____ ☐ 10^6 /µL ☐ 10^{12} /L	☐	☐	☐	☐
☐	☐	HEMOGLOBIN : _____ ☐ g/dL ☐ mmol/L ☐ mg/dL	☐	☐	☐	☐
☐	☐	HEMATOCRIT: _____ %	☐	☐	☐	☐
☐	☐	PLATELET COUNT : _____ 10^3/ µL	☐	☐	☐	☐
☐	☐	COAGULATION PROFILE: INR _____ PTT _____ PT _____				
☐	☐	PLASMA FREE HEMOGLOBIN : _____ ☐ mg/dL ☐ mmol/L ☐ g/dL	☐	☐	☐	☐
		OR				
☐	☐	☐ 10^6 /uL HAPTOGLOBIN : _____ ☐ mg/dL	☐	☐	☐	☐
		OR				
☐	☐	SERUM LDH : _____ ☐ IU/L	☐	☐	☐	☐

DATE SIGNED

_____ **D D M M M Y Y Y Y**

SIGNATURE

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DATE INFORMATION COLLECTED: _____ (DD/MMM/YYYY)

CURRENT MEDICATIONS PLEASE INDICATE WHAT TYPE OF MEDICATIONS THE SUBJECT IS CURRENTLY TAKING:

YES	NO	
☐	☐	ACE OR ARB INHIBITORS
☐	☐	ANTIARRHYTHMICS
		☐ BETA BLOCKERS (PROPANOLOL, ESMOLOL)
		☐ OTHER (SODIUM/ POTASSIUM CHANNEL BLOCKERS—AMIODARONE) SPECIFY: _____
☐	☐	ANTICOAGULANTS
		☐ WARFARIN -- COUMADIN OR DERIVATIVES
		☐ OTHER, SPECIFY: _____
☐	☐	ANTIPLATELETS
		☐ DIPYRIDAMOLE -- PERSANTINE
		☐ ASPIRIN – ECOTRIN OR ENTROPHEN
		☐ TICLOPIDINE -- TICLID
		☐ CLOPIDOGREL --PLAVIX
		☐ OTHER, SPECIFY: _____
☐	☐	CALCIUM BLOCKER
☐	☐	DIURETIC
☐	☐	LIPID LOWERING
☐	☐	NITRATES
☐	☐	STEROIDS

_____ DATE | | | | | | | | | |

SIGNATURE D D M M M Y Y Y Y

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CARDIOVASCULAR MEDICAL HISTORY

YES NO

☐ ☐ **CORONARY ARTERY DISEASE** – (INDICATE WHICH NATIVE CORONARY VESSEL HAS ≥ 50% NARROWING)
- ☐ LEFT ANTERIOR DESCENDING (LAD) CORONARY ARTERY
- ☐ CIRCUMFLEX CORONARY ARTERY
- ☐ RIGHT CORONARY ARTERY
- ☐ LEFT MAIN CORONARY ARTERY

☐ ☐ **CAROTID ARTERY DISEASE** – (INDICATE THE SEVERITY OF DISEASE)
- ☐ CAROTID OCCLUSION (>79% DIAMETER OCCLUSION)
- ☐ ≥ 50% STENOSIS BUT NO OCCLUSION
- ☐ < 50% STENOSIS

☐ ☐ **PERIPHERAL ARTERY /VASCULAR DISEASE** (INDICATE WHICH SYMPTOMS THE SUBJECT HAS EXPERIENCED)
- ☐ CLAUDICATION
- ☐ > 50% STENOSIS BUT OF ANY PERIPHERAL ARTERY
- ☐ AORTIC ANEURYSM

☐ ☐ **PULMONARY HYPERTENSION**

WHAT IS THE SEVERITY OF THE CONDITION?
- ☐ MILD (PULMONARY ARTERY SYSTOLIC PRESSURE <31mmHg)
- ☐ MODERATE (PULMONARY ARTERY SYSTOLIC PRESSURE 31-55mmHg)
- ☐ SEVERE (PULMONARY ARTERY SYSTOLIC PRESSURE IS >55mHg)

☐ ☐ **SYSTEMIC HYPERTENSION**
- ☐ HAS A DOCUMENTED HISTORY OF HYPERTENSION DIAGNOSED AND TREATED WITH MEDICATION, DIET, AND/OR EXERCISE
- ☐ HAS PRIOR DOCUMENTATION OF BLOOD PRESSURE >140 MMHG SYSTOLIC OR 90 MMHG DIASTOLIC FOR PATIENTS WITHOUT DIABETES OR CHRONIC KIDNEY DISEASE; OR PRIOR DOCUMENTATION OF BLOOD PRESSURE >130 MMHG SYSTOLIC OR 80 MMHG DIASTOLIC ON AT LEAST 2 OCCASIONS FOR PATIENTS WITH DIABETES OR CHRONIC KIDNEY DISEASE
- ☐ IS CURRENTLY ON PHARMACOLOGIC THERAPY TO CONTROL HYPERTENSION

☐ ☐ **CARDIOMYOPATHY**
- ☐ PRIMARY/INTRINSIC (HYPERTROPHIC, DILATED, ETC)
- ☐ SECONDARY/EXTRINSIC (ISCHEMIC, DIABETIC, ETC)

☐ ☐ **CONGESTIVE HEART FAILURE**

☐ ☐ **AORTIC STENOSIS**

IF YES:
- ☐ MILD
- ☐ MODERATE
- ☐ SEVERE
- ☐ UNKNOWN

☐ ☐ **AORTIC INSUFFICIENCY**

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☐ +1TRACE
☐ +2 MILD
☐ +3 MODERATE
☐ +4 SEVERE

MITRAL STENOSIS
IF YES:
☐ MILD
☐ MODERATE
☐ SEVERE
☐ UNKNOWN

☐ ☐ **MITRAL INSUFFICIENCY**
☐ +1TRACE
☐ +2 MILD
☐ +3 MODERATE
☐ +4 SEVERE

PULMONARY STENOSIS
IF YES:
☐ MILD
☐ MODERATE
☐ SEVERE
☐ UNKNOWN

☐ ☐ **PULMONARY INSUFFICIENCY**
☐ +1TRACE
☐ +2 MILD
☐ +3 MODERATE
☐ +4 SEVERE
☐ OTHER, SPECIFY: _____

TRICUSPID STENOSIS
IF YES:
☐ MILD
☐ MODERATE
☐ SEVERE
☐ UNKNOWN

☐ ☐ **TRICUSPID INSUFFICIENCY**
☐ +1TRACE
☐ +2 MILD
☐ +3 MODERATE
☐ +4 SEVERE
☐ OTHER, SPECIFY: _____

☐ ☐ **MYCARDIAL INFARCTION** (IF YES, INDICATE TYPE AND DATE OF LAST OCCURRENCE)
☐ STEMI ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (D D / M M M / Y Y Y Y)
☐ NON STEMI ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (D D / M M M / Y Y Y Y)
☐ OTHER ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (D D / M M M / Y Y Y Y)

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☐ UNK ___ ___ / ___ ___ ___ / ___ ___ ___ ___
D D M M M Y Y Y Y

IF DATE IS UNKNOWN, APPROXIMATELY HOW MANY MONTHS AGO DID THE LAST MI OCCUR?

_____MONTHS AGO

IF UNKNOWN, DID THE EVENT OCCUR >5 YEARS AGO? YES ☐ NO ☐

☐ ☐ **CARDIAC RHYTHM ABNORMALITIES/ CONDUCTION DISTURBANCES**

HAS THE SUBJECT EVER HAD THE FOLLOWING CARDIAC RHYTHMS?

- ☐ SINUS TACHYCARDIA
- ☐ SINUS BRADYCARDIA
- ☐ TACHYCARDIA- BRADYCARDIA SYNDROME
- ☐ ATRIAL FIBRILLATION/SUPRAVENTRICULAR TACHYCARDIA
  - ☐ PAROXYSMAL
  - ☐ PERSISTENT

  IS THIS A PERMANENT CONDITION? YES ☐ NO ☐
- ☐ ATRIAL FLUTTER
- ☐ TACHYCARDIA-BRADYCARDIA SYNDROME
- ☐ VENTRICULAR TACHYCARDIA
  - ☐ NONSUSTAINED/PREMATURE VENTRICULAR COMPLEXES
  - ☐ SUSTAINED
- ☐ OTHER CARDIAC ARRHYTHMIA

  PLEASE SPECIFY: _____

HAS THE SUBJECT EVER SHOWN SIGNS OF THE FOLLOWING CONDUCTION DISTURBANCES?

- ☐ **AV BLOCK**

  INDICATE THE LAST RECORDED DEGREE OF AV BLOCK
  - ☐ 1st
  - ☐ 2nd
  - ☐ 3rd
  - ☐ UNKNOWN
- ☐ **BUNDLE BRANCH BLOCK/ INTRAVENTRICULAR BLOCKS**

  INDICATE BRANCH
  - ☐ LEFT- COMPLETE ☐ LEFT-INCOMPLETE
  - ☐ RIGHT- COMPLETE ☐ RIGHT - INCOMPLETE
  - ☐ LEFT ANTERIOR FASCULAR BLOCK
  - ☐ LEFT POSTERIOR FASICULAR BLOCK
  - ☐ NONSPECIFIC INTRAVENTRICULAR CONDUCTION DEFECTS
- ☐ **OTHER CONDUCTION DISTURBANCE** _____

☐ ☐ **TRANSIENT ISCHEMIC ATTACK (TIA; RECOVERED WITHIN 24 HOURS)**
IS THE DATE WHEN THE LAST KNOWN TIA OCCURRED KNOWN?

DATE: _____ (DD/MMM/YYYY)

IF DATE IS UNKNOWN, APPROXIMATELY HOW MANY MONTHS AGO DID THE LAST MI OCCUR?

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_____MONTHS AGO

IF UNKNOWN, DID THE EVENT OCCUR >5 YEARS AGO? YES ☐ NO ☐

☐ ☐ **CEREBROVASCULAR ACCIDENT (CVA/STROKE; DID NOT RECOVER WITHIN 24 HOURS)**

(IF YES, INDICATE TYPE OF EVENTS AND DATE OF LAST OCCURRENCE)

☐ DATE OF LAST KNOWN CVA

__ __ / __ __ __ / __ __ __ __
D D M M M Y Y Y Y

IF DATE IS UNKNOWN, APPROXIMATELY HOW MANY **WEEKS** AGO DID THE LAST TIA OCCUR?

_____WEEKS AGO

IF UNKNOWN, DID THE EVENT OCCUR >5 YEARS AGO? YES ☐ NO ☐

DOES THE SUBJET HAVE SEVERE IMPAIRMENT OF MOBILITY AS A RESULT OF A NEUROLOGICAL DYSFUNCTION? YES ☐ NO ☐

☐ ☐ **ENDOCARDITIS**

- ☐ CURENTLY BEING TREATED
- ☐ TREATED WITHIN THE LAST 3 MONTHS (NOT CURRENTLY BEING TREATED)
- ☐ TREATED > 3 MONTHS AGO

☐ ☐ **MYOCARDITIS**

- ☐ CURENTLY BEING TREATED
- ☐ TREATED WITHIN THE LAST 3 MONTHS (NOT CURRENTLY BEING TREATED)
- ☐ TREATED > 3 MONTHS AGO

☐ ☐ **HYPERLIPIDEMIA OR HYPERCHOLESTEROLEMIA**

☐ ☐ **RHEUMATIC FEVER**

PRIOR CARDIOVACULAR SURGICAL INTERVENTIONS

HOW MANY CARDIOVASCULAR SURGERIES HAS THE SUBJECT PREVIOUSLY HAD? (Any vascular intervention including CABG, PTCA, Stent, PCI, Endarterectomy, endovascular angioplasties)

- ☐ 0
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ ≥ 4

HOW MANY CARDIAC/HEART SURGERIES HAS THE SUBJECT PREVIOUSLY HAD? (Valve replacements/ repairs/ valvuloplasties/ commisurotomies/ ASD and PFO repairs, MAZE/ablation procedures)

- ☐ 0
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ ≥ 4

HAS THE SUBJECT REQUIRED AMPUTATION OF A LIMB DUE TO ARTERIAL DISEASE? YES ☐ NO ☐

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HAS THE SUBJECT BEEN IMPLANTED WITH A PERMANENT PACEMAKER OF AN IMPLANTABLE CARDIOVERTER DEFRIBRILLATOR?

Yes **No**

☐ ☐ AICD / PACEMAKER IMPLANT

SPECIFY THE TYPE OF IMPLANT THE SUBJECT HAS:

- ☐ INTERMITTANT (RATE-RESPONSIVE/ON DEMAND) PACEMAKER
- ☐ CONTINUOUS PACEMAKER
- ☐ ICD/AICD

IF YES, INDICATE DATE OF IMPLANT ___ ___ / ___ ___ ___ / ___ ___ ___ ___
D D M M M Y Y Y Y

IF DATE IS UNKNOWN, APPROXIMATELY HOW MANY MONTHS AGO WAS THE SUBJECT IMPLANTED?

_____MONTHS AGO

IF UNKNOWN, DID THE EVENT OCCUR >5 YEARS AGO? YES ☐ NO ☐

WERE SURGICAL INTERVENTIONS PERFORMED ON ANY OF THE FOLLOWING CARDIOVASCULAR COMPONENTS?

☐ ☐ **CAROTID ARTERIES**

WHAT TYPES OF INTERVENTION WAS DONE ON THE CAROTIDS?

- ☐ ENDARTERECTOMY
- ☐ ENDOVASCULAR ANGIOPLASTY AND STENTING
- ☐ OTHER INTERVENTION ON THE CAROTIDS: _____

☐ ☐ **ABDOMINAL AORTA**

☐ ☐ **THORACIC AORTA**

☐ ☐ **LIMB ARTERIES**

☐ ☐ **CORONARY ARTERIES**

WHAT TYPE OF INTERVENTIONS HAVE BEEN PERFORMED?

CABG YES ☐ NO ☐

- ☐ 1 GRAFT ☐ 2 GRAFTS
- ☐ 3 GRAFTS ☐ 4 GRAFTS
- ☐ UNKNOWN

PTCA (BALLOON ANGIOPLASTY)/ PERCUTANEOUS CORONARY INTERVENTION (PTCI) YES ☐ NO ☐

WAS A STENT EMPLOYED FOR ANY OF THE PAST PTCA/PTCI PROCEDURES? YES ☐ NO ☐

OTHER INTERVENTION ON THE CORONARY ARTERIES: YES ☐ NO ☐

_____

☐ ☐ **AORTIC VALVE**

- ☐ VALVULOPLASTY
- ☐ VALVE REPLACEMENT
- ☐ OTHER REPAIR:_____

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☐ ☐ **MITRAL VALVE**

- ☐ ANNULOPLASTY
- ☐ VALVULOPLASTY
- ☐ VALVE REPLACEMENT
- ☐ OTHER REPAIR:_____

☐ ☐ **PULMONARY VALVE**

- ☐ VALVULOPLASTY
- ☐ VALVE REPLACEMENT
- ☐ OTHER REPAIR:_____

☐ ☐ **TRICUSPID VALVE**

- ☐ ANNULOPLASTY
- ☐ VALVULOPLASTY
- ☐ VALVE REPLACEMENT
- ☐ OTHER REPAIR:_____

☐ ☐ **OTHER CARDIOVASCULAR COMPONENT, SPECIFY (LOCATION AND TYPE OF PROCEDURE PERFORMED):**

_____

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NON-CARDIOVASCULAR RISK FACTORS

DOES THE SUBJECT CURRENTLY HAVE OR HAS THE SUBJECT EVER HAD THE FOLLOWING DISEASES?

YES	NO	
☐	☐	**BLEEDING DIATHESIS**

☐ ACUTE ANEMIA (HEMOGLOBIN <10.0G/DL OR 6.2 MMOL/L)
☐ BLEEDING DIATHESIS
☐ COAGULOPATHIES
☐ LEUKOPENIA (WBC <3.5 x 10^3/ uL)
☐ THROMBOCYTOPENIA (PLATELET COUNT < 50 x 10^3 /uL)
☐ OTHER TYPE, SPECIFY: _____

☐	☐	**CALCIUM METABOLIC DISORDERS**
☐	☐	**CANCER**, SPECIFY: _____

HAS THE SUBJECT RECEIVED OR WILL THE SUBJECT RECEIVE CHEMOTHERAPY WITHIN 30 DYAS PRIOR TO THE STUDY PROCEDURE? YES ☐ NO ☐

☐	☐	**CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)/ CHRONIC LUNG DISEASE**

PLEASE INDICATE THE FEV1/FVC VALUE:
☐ 60-75%
☐ 50-59%
☐ <50%
☐ NOT AVAILABLE

WHAT TREATMENT DID THE SUBJECT RECEIVE FOR THIS CONDITION?
☐ CHRONIC INHALED OR ORAL BRONCHODILATOR THERAPY
☐ CHRONIC STEROID THERAPY
☐ OXYGEN OR VENTILATION
☐ OTHER TREATMENT (SPECIFY) _____

☐	☐	**DIABETES**

☐ TYPE 1
☐ TYPE 2 (INDICATE WHAT TREATMENT THE PATIENT IS RECEIVING)
☐ NONE ☐ DIET ☐ ORAL ☐ INSULIN

☐	☐	**OBESITY** (BMI ≥ 30)
☐	☐	**LIVER DISEASE**
☐	☐	**MUSCULOSKELETAL DYSFUNCTION**

DOES THE SUBJECT HAVE SEVERE IMPAIRMENT OF MOBILITY DUE TO THIS CONDITION? YES ☐ NO ☐

☐	☐	**RENAL FAILURE / INSUFFICIENCY**

DATE SUBJECT WAS DIAGNOSED:

__ __ / __ __ __ / __ __ __ __
D D M M M Y Y Y Y

IF UNKNOWN, APPROXIMATELY HOW MANY MONTHS AGO WAS THE SUBJECT DIAGNOSED? _____

IF UNKNOWN, WAS THE SUBJECT DIAGNOSED > 5 YEARS AGO? YES ☐ NO ☐

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YES ☐ NO ☐ SUBJECT CURRENTLY RECEIVING DIALYSIS

☐ ☐ OTHER DISEASE WHICH REQUIRES IMMUNOSUPPRESIVE THERAPY INHALED OR SYSTEMIC STEROID THERAPY OR CHEMOTHERAPY WITHIN 30 DAYS OF THE STUDY PROCEDURE

☐ ☐ **SMOKER, CURRENT**

IF NO, WHEN DID SUBJECT QUIT:

☐ QUIT > 1 MONTH AGO

☐ QUIT ≤ 1 MONTH AGO

☐ ☐ **ALCOHOL/DRUG ABUSE**

SIGNATURE

DATE ☐☐ ☐☐☐ ☐☐☐☐

D D M M M Y Y Y Y

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QualityMetric's SF-12v2® Health Survey[1] is a shorter version of the SF-36v2® Health Survey that uses just 12 questions to measure functional health and well-being from the subject's point of view. It takes only 2-3 minutes to complete. The SF-12v2 is a practical, reliable, and valid measure of physical and mental health and covers the same eight health domains as the SF-36v2 with one or two questions per domain.

Date of Assessment: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
D D M M M Y Y Y Y

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
❑1	❑2	❑3	❑4	❑5

2. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.	❑1	❑2	❑3
b. Climbing several flights of stairs.	❑1	❑2	❑3

3. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Accomplished less than you would like.	❑1	❑2	❑3	❑4	❑5
b. Were limited in the kind of work or other activities.	❑1	❑2	❑3	❑4	❑5

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

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	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Accomplished less than you would like.	❑1	❑2	❑3	❑4	❑5
b. Did work or activities less carefully than usual?	❑1	❑2	❑3	❑4	❑5

5. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all ❑1 | A little bit ❑2 | Moderately ❑3 | Quite a bit ❑4 | Extremely ❑5

6. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks ……

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Have you felt calm and peaceful?	❑1	❑2	❑3	❑4	❑5
b. Did you have a lot of energy?	❑1	❑2	❑3	❑4	❑5
c. Have you felt downhearted and depressed?	❑1	❑2	❑3	❑4	❑5

7. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time ❑1 | Most of the time ❑2 | Some of the time ❑3 | A little of the time ❑4 | None of the time ❑5

SIGNATURE

DATE SIGNED | | | | | | | | | |
D D M M M Y Y Y Y

[1]SF-12v2™ Health Survey© 1994, 2002 by QualityMetric incorporated and Medical Outcomes Trust.
SF-12® a registered trademark of Medical Outcomes Trust. (SF12v2 Standard, US version 2.0).

ECHO SITE TRACKING FORM

Date ECHO exam __ __ / __ __ __ / __ __ __ __ (DD/MMM/YYYY)

Name of the echocardiographer _____

Echocardiograph equipment used (check one):

☐ GE Vivid

☐ Other GE, specify _____

☐ Philips IE33

☐ Other Philips, specify: _____

☐ Siemens

☐ Other model, specify: _____

Please provide the following physical assessment parameters:

Subject weight _____ ☐ kg ☐ lb

Heart rate _____ bpm

Blood pressure _____ / _____ mmHg

Cardiac rhythm (check one):

☐ NSR ☐ Afib ☐ Paced ☐ Indeterminate

Miscellaneous

Is subject enrolled in aortic or mitral arm of trial?

☐ AORTIC ☐ MITRAL

Did the echocardiographer assess the study valve?

☐ No ☐ Yes

Date echocardiographs shipped/uploaded to the Core Lab __ __ / __ __ __ / __ __ __ __ (DD/MMM/YYYY)

Shipping

Shipping method (check one):

☐ Images uploaded

☐ Fed Ex

☐ UPS

☐ DHL

☐ Other provider, specify: _____

Shipping tracking number: _____

Comments:

_____ DATE | | | | | | | | | |

SIGNATURE D D M M M Y Y Y Y

ECHO SITE EVALUATION FORM

Please indicate the results of the LVOT assessment:

Peak velocity		m/sec	☐ Not evaluable
Peak gradient		mmHg	☐ Not evaluable
Mean gradient		mmHg	☐ Not evaluable
VTI		cm	☐ Not evaluable

Please indicate the results of the **AORTIC OR MITRAL** valve assessment (complete section for trial arm position):
Please only indicate results **POST-implant of the valve for the operative TEE

Peak velocity		m/sec	☐ Not evaluable
Peak gradient		mmHg	☐ Not evaluable
Mean gradient		mmHg	☐ Not evaluable
VTI		cm	☐ Not evaluable
Annulus size		cm	☐ Not evaluable
Valve area		cm^2	☐ Not evaluable

Please indicate the AR severity:

- ☐ 0 None
- ☐ +1 Trivial/Trace
- ☐ +2 Mild
- ☐ +3 Moderate
- ☐ +4 Severe
- ☐ Indeterminate

Please indicate the MR severity:

- ☐ 0 None
- ☐ +1 Trivial/Trace
- ☐ +2 Mild
- ☐ +3 Moderate
- ☐ +4 Severe
- ☐ Indeterminate

LVEF		%	☐ Not evaluable
LVEF range (max, min)	-	%	☐ Not evaluable

What method was used for LVEF?

- ☐ Single plane
- ☐ Biplane
- ☐ Quinones
- ☐ Visual

Please indicate the severity of paravalvular leak (PVL) of the study valve:

- ☐ 0 None
- ☐ +1 Trivial/Trace
- ☐ +2 Mild
- ☐ +3 Moderate
- ☐ +4 Severe
- ☐ Indeterminate
- ☐ Not applicable at baseline

What was the assessment of RV function?

- ☐ Normal
- ☐ Mildly reduced
- ☐ Moderately reduced
- ☐ Severely reduced
- ☐ Indeterminate

SIGNATURE

DATE _ _ _ _ _ _ _ _ _

D D M M M Y Y Y Y

COMMENCE™ TRIAL – MODELS 11000A AND 11000M

Subject Study ID **201202** ☐☐☐-☐☐☐ Site# ☐☐☐

DATE OF HOSPITAL ADMISSION: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
D D M M M Y Y Y Y

DATE OF SURGERY: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
D D M M M Y Y Y Y

IMPLANTING SURGEON: _____

PREOPERATIVE CONDITION

YES	NO	
☐	☐	**DID A MYOCARDIAL INFARCTION (MI) OCCUR WITHIN 21 DAYS PRIOR TO SURGERY?** INDICATE THE TIME INTERVAL WHEN THE LAST MI OCCURRED: ☐ <6 HOURS ☐ 6-24 HOURS ☐ 1-7 DAYS ☐ 8-21 DAYS
☐	☐	**WITHIN 2 WEEKS PRIOR TO THE SURGICAL PROCEDURE: WAS THE SUBJECT IN CONGESTIVE HEART FAILURE?**
☐	☐	**WITHIN 2 WEEKS PRIOR TO THE SURGICAL PROCEDURE: DID THE SUBJECT EXPERIENCE AN ARRHYTHMIA?** WAS THE OBSERVED ARRHYTHMIA CONSIDERED ATRIAL FIBRILLATION OR ATRIAL FLUTTER? ☐ YES ☐ NO
☐	☐	**WAS THE SUBJECT EXPERIENCING CARDIAC/CHEST PAIN AT ADMISSION?** WHAT IS THE LIKELY CAUSE OF THESE SYMPTOMS? ☐ STABLE ANGINA ☐ UNSTABLE ANGINA ☐ UNLIKELY DUE TO ISCHEMIA ☐ NON-STEMI ☐ STEMI
☐	☐	**DID THE SUBJECT RECEIVE IV INOTROPIC AGENTS WITHIN 48 HOURS PRECEDING SURGERY OR ADMINISTRATION OF THIS MEDICATION DOCUMENTED AS CONTRAINDICATED?**

DID THE SUBJECT EXPERIENCE OR REQUIRE ANY OF THE FOLLOWING AFTER ADMISSION BUT PRIOR TO GOING UNDER ANESTHESIA?:

☐	☐	VENTRICULAR FIBRILLATION
☐	☐	VENTRICULAR TACHYCARDIA
☐	☐	CARDIOGENIC SHOCK
☐	☐	ABORTED SUDDEN DEATH
☐	☐	ACUTE RENAL FAILURE (ANURIA OR OLIGURIA <10 ML/HR)
☐	☐	CARDIOPULMONARY RESUSCITATION < 1 HOUR PRIOR TO SURGERY
☐	☐	VENTILATION PRIOR TO ARRIVAL IN THE ANESTHETIC ROOM
☐	☐	INOTROPIC SUPPORT OR IABP
☐	☐	ANOTHER CARDIAC INTERVENTION <6 HOURS PRIOR TO SCHEDULED SURGERY

WHAT IS THE URGENCY OF THE SURGERY BEING PERFORMED? (CHECK ONE)

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- ☐ ELECTIVE
- ☐ URGENT
- ☐ SALVAGE
- ☐ EMERGENCY

PLEASE CONFIRM THE DIAGNOSIS FOR THE CURRENT REPLACEMENT (CHECK ONE)

- ☐ STENOSIS
- ☐ STENOSIS WITH INSUFFICIENCY
- ☐ PURE INSUFFICIENCY
- ☐ PROSTHETIC VALVE DYSFUNCTION
- ☐ OTHER DIAGNOSIS, SPECIFY: _____

SURGICAL APPROACH (CHECK ONE)

- ☐ FULL STERNOTOMY
- ☐ MINI UPPER STERNOTOMY
- ☐ RIGHT THORACOTOMY
- ☐ OTHER MIS, SPECIFY: _____

SURGICAL APPROACH AND ANNULUS PREPARATION

WERE THE FOLLOWING CONCOMITANT PROCEDURES PERFORMED?

YES	NO	
☐	☐	**CORONARY ARTERY BYPASS GRAFTNG (CABG = Distal anastomosis)**

HOW MANY GRAFTS WERE DONE?

☐ *1* ☐ *2* ☐ *3* ☐ *4+*

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YES **NO**

☐ ☐ **PERMANENT PACEMAKER IMPLANT**

WAS CARDIAC RESYNCHRONIZATION TECHNIQUE (CRT) USED?

☐ YES ☐ NO

WAS THIS PROCEDURE PLANNED?

☐ YES ☐ NO

IF NO, WHY WERE TEMOPRARY PACER LINES NOT EMPLOYED?

_____

☐ ☐ **AUTOMATED IMPLANTED CARDIOVERTER (AICD) IMPLANT**

WAS CARDIAC RESYNCHRONIZATION TECHNIQUE (CRT) USED?

☐ YES ☐ NO

☐ ☐ **ATRIAL ABLATION**

WHAT TYPE OF ABLATION PROCEDURE WAS DONE?

☐ PRIMARY EPICARDIAL

☐ PRIMARILY INTRACARDIAC

☐ ☐ **AORTIC ANEURYSM/ DISSECTION REPAIR**

☐ ☐ **ATRIAL SEPTAL DEFECT (ASD) REPAIR**

WHAT WAS THE TYPE OF DEFECT REPAIRED?

☐ PATENT FORAMEN OVALE

☐ SECUNDUM ASD

☐ SINUS VENOSUS ASD

☐ MULTIPLE DEFECTS

☐ ☐ **ROOT SINUS ENLARGEMENT**

☐ ☐ **AORTIC ANNULAR ENLARGMENT**

WHAT METHOD WAS USED?

☐ NICKS

☐ MANOUGUIAN

☐ KONNO

☐ ☐ **TRICUSPID VALVE REPAIR (WITH MITRAL VALVE REPLACEMENT)**

☐ ☐ **OTHER PROCEDURE,** PLEASE SPECIFY: _____

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YES **NO**

☐ ☐ **WERE ANY UNPLANNED PROCEDURES PERFORMED DURING THIS OPERATION?**

WHY WAS THIS PROCEDURE NECESSARY?

- ☐ UNSUSPECTED SUBJECT DISEASE OR ANATOMY
- ☐ SURGICAL COMPLICATION

☐ ☐ **WAS AN INTRAAORTIC BALLOON PUMP (IABP) USED IN RELATION TO THIS SURGICAL PROCEDURE? ?**

WHEN WAS THE IABP INSERTED?

- ☐ PREOPERATIVELY
- ☐ INTRAOPERATIVELY
- ☐ POSTOPERATIVELY

☐ ☐ **WAS ANNULAR DEBRIDEMENT PERFORMED?**

DEGREE:

- ☐ ROUTINE
- ☐ EXTENSIVE – NOT REQUIRING ANNULAR REPAIR
- ☐ EXTENSIVE – REQUIRING ANNULAR REPAIR/RECONSTRUCTION

LOCATION:

- ☐ FULL ANNULAR CIRCUMFERENCE
- ☐ PARITAL ANNULAR CIRCUMFERENCE (>= 50%)
- ☐ PARTIAL ANNULAR CIRCUMFERENCE (<50%)

CALCIFICATION REMOVAL:

- ☐ COMPLETE
- ☐ INCOMPLETE (>= 50%)
- ☐ INCOMPLETE (<50%)

WHAT STUDY VALVE MODEL WAS EMPLOYED? (CHECK ONE)

- ☐ **11000A**
- ☐ **11000M**

HOW MANY ATTEMPTS WERE MADE TO IMPLANT THE VALVE? (CHECK ONE)

- ☐ **2**
- ☐ **1**

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WHY WAS A SECOND ATTEMPT TO IMPLANT THE STUDY VALVE NOT PERFORMED?

- ☐ FIRST ATTEMPT SUCCESSFUL
- ☐ A STUDY VALVE OF THE CORRECT SIZE IS NOT AVAILABLE AT THE SITE
- ☐ NONE OF THE SIZES AVAILABLE FOR THE STUDY VALVE ARE SUITABLE FOR THE SUBJECT
- ☐ SURGEON CHOSE NOT TO ATTEMPT TO IMPLANT THE STUDY VAVLE AGAIN DUE TO A MEDICAL COMPLICATION
- ☐ OTHER REASON: SPECIFY: _____

WAS THE HEART RESTARTED WITH THE STUDY VALVE IMPLANTED?

☐ **NO**

WAS A COMMERCIAL VALVE SUCCESSFULLY IMPLANTED?

- ☐ **NO (PLEASE FILL OUT A STUDY EXIT FORM)**
- ☐ **YES**

PLEASE PROVIDE THE FOLLOWING INFORMATION ABOUT THE COMMERCIAL VALVE:

MANUFACTURER AND MODEL: _____

VALVE SIZE (MM): _____

SERIAL NUMBER: _____

☐ **YES**

WAS A POST-IMPLANT TRANSESOPHAGEAL ECHOCARDIOGRAM PERFORMED?

- ☐ **NO**
- ☐ **YES**

TIME ECHOCARDIOGRAM STARTED: | | | : | | | (24 HR FORMAT)

WHAT TYPE OF ECHOCARDIOGRAM WAS DONE?

☐ TEE ☐ TTE

WAS ANY OBSERVED REGURGITATON CLINICALLY ACCEPTABLE?

☐ NO ☐ YES

WAS SERUM GLYCEROL ANALYSIS REQUIRED FOR THIS SUBJECT?

☐ NO ☐ YES

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WAS A POST-OPERATIVE ELECTROCARDIOGRAM PERFORMED UPON ARRIVAL TO THE ICU?

☐ NO ☐ YES

YES	NO	
☐	☐	**WAS THERE A BLEEDING-RELATED REOPERATION WITHIN THE FIRST 24 HOURS AFTER SURGERY?**
☐	☐	**DID ANY ADVERSE EVENTS OCCUR DURING SURGERY?** IF YES, COMPLETE ADVERSE EVENT (AE) FORM (S)

SURGICAL PROCEDURE TIMING

SKIN INCISION:			:		(24 HR FORMAT)
START ECC (PUMP):			:		(24 HR FORMAT)
START CROSS CLAMP:			:		(24 HR FORMAT)
START SIZING:			:		(24 HR FORMAT)
REMOVAL CROSS CLAMP:			:		(24 HR FORMAT)
END ECC (PUMP):			:		(24 HR FORMAT)
SKIN CLOSURE:			:		(24 HR FORMAT)

COMMENTS:

SIGNATURE

DATE SIGNED | | | | | | | | | |

D D M M M Y Y Y Y

Subject Study ID **201202** | | | | - | | | | Site# | | | |

AORTIC VALVE ETIOLOGY

YES	NO	
☐	☐	DEGENERATIVE
☐	☐	DYSTROPHIC CALCIFICATION
☐	☐	CONGENITAL
☐	☐	RHEUMATIC
☐	☐	REMOTE ENDOCARDITIS
☐	☐	OTHER ETIOLOGY, SPECIFY: _____

CONDITION OF THE AORTIC VALVE AND SURROUNDING ANATOMY

YES	NO	
☐	☐	WAS CALCIFICATION OBSERVED?

YES	NO	
☐	☐	ANNULUS
☐	☐	LEAFLETS
☐	☐	AORTIC WALL
☐	☐	CORONARY ARTERIES
☐	☐	LEAFLET FUSION
☐	☐	LEAFLET PERFORATION
☐	☐	MYXOMATOUS (LEAFLET)
☐	☐	VEGETATION
☐	☐	CONGENITAL VALVE DEFECT
		☐ BICUSPID AORTIC VALVE
		☐ UNICUSPID AORTIC VALVE
☐	☐	OTHER DISEASE CONDITION, SPECIFY: _____

COMMENTS:

SIGNATURE

DATE SIGNED | | | | | | | | | |

D D M M M Y Y Y Y

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MITRAL VALVE ETIOLOGY

YES	NO	
☐	☐	DEGENERATIVE
☐	☐	DYSTROPHIC CALCIFICATION
☐	☐	FUNCTIONAL DISEASE
☐	☐	CONGENITAL
☐	☐	RHEUMATIC
☐	☐	REMOTE ENDOCARDITIS
☐	☐	ISCHEMIC HEART DISEASE
☐	☐	MITRAL VALVE PROLAPSE

- ☐ ANTERIOR
- ☐ POSTERIOR
- ☐ BILEAFLET

☐ ☐ OTHER ETIOLOGY, SPECIFY: _____

CONDITION OF THE MITRAL VALVE AND SURROUNDING ANATOMY

YES **NO**

☐ ☐ WAS CALCIFICATION OBSERVED?

YES	NO	
☐	☐	ANNULUS

- ☐ ANTERIOR
- ☐ POSTERIOR
- ☐ BILATERAL

☐	☐	LEAFLETS

- ☐ ANTERIOR
- ☐ POSTERIOR
- ☐ BILEAFLET

☐	☐	CHORDAE TENDINAE
☐	☐	PAPILLARY MUSCLE
☐	☐	DILATED ANNULUS
☐	☐	LEAFLET FUSION
☐	☐	LEAFLET PERFORATION
☐	☐	MYXOMATOUS (LEAFLET)
☐	☐	FIBROELASTIC DEFICIENCY
☐	☐	VEGETATION
☐	☐	CONGENITAL MITRAL VALVE DEFECT

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YES	NO	
☐	☐	CHORDAE DYSFUNCTION
		☐ ELONGATED
		☐ TETHERED
		☐ RUPTURED
☐	☐	OTHER DISEASE CONDITION, SPECIFY:_____

MITRAL VALVE REPLACEMENT TECHNIQUE

ANTERIOR LEAFLET

- ☐ COMPLETE PRESERVATION
- ☐ PARTIAL PRESERVATION
- ☐ COMPLETE REMOVAL

POSTERIOR LEAFLET

- ☐ COMPLETE PRESERVATION
- ☐ PARTIAL PRESERVATION
- ☐ COMPLETE REMOVAL

ANTERIOR CHORDS

- ☐ PRESERVED
- ☐ REMOVED

POSTERIOR CHORDS

- ☐ PRESERVED
- ☐ REMOVED

COMMENTS:

DATE SIGNED | | | | | | | | |

SIGNATURE

D D M M M Y Y Y Y

What study valve implant attempt was being performed? ☐ 1st attempt ☐ 2nd attempt

Please provide the following information about the study valve:

Valve size:

☐ 19mm ☐ 21mm ☐ 23mm ☐ 25mm ☐ 27mm ☐ 29mm ☐ 31mm ☐ 33mm

Serial Number: _____

What type of sizer was used?

☐ Model 1133 [AORTIC]

☐ Model 1173 [MITRAL]

☐ Universal sizer

☐ Other sizer, specify: _____

What was the barrel size of the valve sizer? _____ mm

What suture technique was used to secure the valve (check one)?

☐ Single simple interrupted without pledgets

☐ Horizontal interrupted mattress without pledgets (intra-annular)

☐ Horizontal interrupted without pledgets (supra-annular)

☐ Horizontal interrupted with pledgets (intra-annular)

☐ Horizontal interrupted with pledgets (supra-annular)

☐ Continuous running sutures without pledgets/strip

☐ Continuous running sutures with pledgets/strip

☐ Interrupted figure of eight without pledgets

☐ Other technique, specify: _____

☐ Not attempted

How was the valve positioned? ☐ Supra-annular ☐ Intra-annular ☐ Not attempted

Did the study valve perform as intended? ☐ No ☐ Yes

Please indicate the types of valve failures observed (select all that apply):

☐ Device function, unable to place sutures through the sewing ring

☐ Device function, unable to position on the aortic annulus

☐ Device function, bioprosthesis and holder separate during procedure

☐ Device function, other, specify: _____

☐ Device use, sizing technique

☐ Device use, sterility compromised

☐ Device use, used expired product

☐ Device use, component damaged by operator

☐ Device use, improper postioning

☐ Device use, other, specify: _____

DEVICE TECHNICAL SUCCESS

Was the heart restarted with the valve in place after this implant attempt? ☐ No ☐ Yes

Did the subject leave the operating room with the study valve in place for this attempt? ☐ No ☐ Yes

If No, Why did the implant attempt fail?

☐ Valve failure (Please indicate the valve failure type on this form)

☐ Subject died

☐ Other reason, specify: _____

Please provide the time at which each step in the study device procedure occurred in HH:MM:SS format:

Start of study procedure (first stitch placed)	__ : __ : __	☐ Not attempted ☐ Not available
First stitch placed on valve ring	__ : __ : __	☐ Not attempted ☐ Not available
Complete the study procedure (last stitch tied down on the valve)	__ : __ : __	☐ Not attempted ☐ Not available

Comments:

_____ DATE SIGNED __ __ __ __ __ __ __ __

SIGNATURE D D M M M Y Y Y Y

Subject Study ID **201202** ☐☐☐-☐☐☐ Site# ☐☐☐

VISIT TYPE: ☐ DISCHARGE ☐ 10 DAY FOLLOW UP (ECHO REQUIRED)

DATE OF DISCHARGE: __ __ / __ __ __ / __ __ __ __
D D M M M Y Y Y Y

DISCHARGED TO:

- ☐ HOME
- ☐ ANOTHER HOSPITAL
- ☐ EXTENDED CARE

POST OPERATIVE HOSPITALIZATION INFORMATION

DURATION OF TIME IN INTENSIVE CARE UNIT _____ DAYS AND _____HOURS

DURATION FO TIME IN INTERMEDIATE CARE / HIGH DEPENDENCY UNIT _____ DAYS AND _____HOURS

DURATION OF TIME IN GENERAL WARD _____ DAYS AND _____HOURS

********COMPLETE ASSESSMENT FORM**********

_____ DATE SIGNED ☐☐ ☐☐☐ ☐☐☐☐
SIGNATURE D D M M M Y Y Y Y

Subject Study ID **201202** | | | | - | | | | Site# | | | |

RECORD ONLY ONE ADVERSE EVENT PER FORM

1. **EVENT ONSET DATE** | | | | | | | | | | (D D M M M Y Y Y Y)

2. **SITE AWARENESS DATE** | | | | | | | | | | (D D M M M Y Y Y Y)

3. **TIMING OF EVENT ONSET** ☐ INTRA-OPERATIVE ☐ POST-OPERATIVE

4. **IS THIS A NEW OR WORSENING ADVERSE EVENT?** ☐ NEW ☐ WORSENING

5. **EVENT NAME**
(SEE ADVERSE EVENT LISTING*) _____

6. **EVENT SUMMARY** _____
_____
_____

7. **METHOD OF DETECTION (**CHECK ALL THAT APPLY) ☐ LAB FINDING ☐ ECHO ☐ ANGIOGRAM ☐ MRI ☐ ECG
☐ AUTOPSY ☐ OBSERVATION ☐ EXAM ☐ REOPERATION
(Date of reoperation:_____ (DD/MMM/YYYY)

☐ OTHER (SPECIFY) _____

DATE OF TEST/ EXAM: _____

8. **CAUSALITY: IS THIS EVENT RELATED TO ANY OF THE FOLLOWING?**

SURGICAL PROCEDURE	☐ YES	☐ NO	☐ UNDETERMINED
STUDY VALVE	☐ YES	☐ NO	☐ UNDETERMINED
STUDY VALVE PROCEDURE	☐ YES	☐ NO	☐ UNDETERMINED
USER ERROR	☐ YES	☐ NO	☐ UNDETERMINED
DEFICIENCY IN INSTRUCTIONS	☐ YES	☐ NO	☐ UNDETERMINED
UNDERLYING CONDITION	☐ YES	☐ NO	☐ UNDETERMINED

IF YES, WHAT WAS THE UNDERLYING CONDITION: _____

9. **DID ANTITHROMBOEMBOLIC MEDICATION CONTRIBUTETO EVENT?**
☐ YES ☐ NO
☐ ANTICOAGULANT MEDICATION
☐ ASPIRIN
☐ OTHER ANTIPLATELET MEDICATION
☐ OTHER ANTITHROMBOEMBOLIC MEDICATION: _____

WAS THIS MEDICATION PRESCRIBED DUE TO THE IMPLANT?
☐ YES ☐ NO

DID NON- ANTITHROMBOEMBOLIC MEDICATION CONTRIBUTE TO EVENT?
☐ YES ☐ NO
IF YES, SPECIFY:_____

10. **SERIOUS ADVERSE EVENT** ☐ YES ☐ NO
☐ RESULTED IN DEATH
☐ RESULTED IN LIFE-THREATENING ILLNESS OR INJURY
☐ RESULTED IN PERMANENT IMPAIRMENT

Subject Study ID **201202** | | | | - | | | | Site# | | | |

- ☐ RESULTED IN HOPSITALIZATION OR PROLONGING OF CURRENT HOSPITALIZATION
- ☐ RESULTED IN SURGICAL INTERVENTION TO PREVENT PERMANENT IMPAIRMENT TO BODY STRUCTURE OR FUNCTION
- ☐ RESULTED IN FETAL DISTRESS OR DEATH, CONGENITAL ABNORMALITY OR BIRTH DEFECT
- ☐ RESULTED IN MEDICAL INTERVENTION TO PREVENT PERMANENT IMPAIRMENT TO BODY STRUCTURE OR FUNCTION

UNANTICIPATED DEVICE RELATED ADVERSE DEVICE EFFECT? ☐ YES ☐ NO

11. ACTION TAKEN/TREATMENT (*MULTIPLE RESPONSES POSSIBLE*)

- ☐ CARDIOVERSION
- ☐ TRANSFUSION

  IF YES, NUMBER OF PRBC UNITS TRANSFUSED_____
- ☐ MEDICATION GIVEN, SPECIFY
- ☐ PACEMAKER/ICD IMPLANT (NOT PLANNED PRIOR TO AVR - PROVIDE DATE) _____ (DD/MMM/YYYY)
- ☐ PROLONGED HOSPITALIZATION
- ☐ RE-HOSPITALIZATION REQUIRED

  ADMISSION DATE: _____ (DD/MMM/YYYY)

  IF SUBJECT DISCHARGED, DISCHARGE DATE: _____ (DD/MMM/YYYY)
- ☐ SURGICAL INTERVENTION, REOP ON STUDY VALVE OR OTHER INTERVENTION ON STUDY VALVE (COMPLETE EXPLANT REPORT)
- ☐ OTHER INVASIVE INTERVENTION (NOT REOPERATION ON STUDY VALVE) (*SPECIFY BELOW – PROVIDE DATE*) | | | | | | | | | | (D D M M M Y Y Y Y)

  SPECIFY OTHER INVASIVE INTERVENTION _____

12. OUTCOME

- ☐ ONGOING
- ☐ UNRESOLVED AT STUDY EXIT
- ☐ UNKNOWN AT STUDY EXIT
- ☐ CHRONIC CONDITION
- ☐ RESOLVED WITH OUT SEQUELAE DATE: | | | | | | | | | | (D D M M M Y Y Y Y)
- ☐ RESOLVED WITH SEQUELAE DATE: | | | | | | | | | | (D D M M M Y Y Y Y)
- ☐ DEATH (PRIMARY CAUSE)
- ☐ DEATH (NOT PRIMARY CAUSE)

_____ DATE SIGNED | | | | | | | | | |

SIGNATURE (D D M M M Y Y Y Y)

Subject Study ID	**201202**				-				Site#			

*AE Categories include:

Blood and lymphatic (including ALL bleeding complications)

Cardiovascular –Arrhythmia

Cardiovascular - Regurgitation

Cardiovascular - Stenosis

Cardiovascular - Embolic Event/Valve Thrombosis

Cardiovascular - Misc

Device Dysfunction

Gastrointestinal/Hepatic

Genitourinary/Renal

Pulmonary/Respiratory

Peripheral Vascular

Psychiatric

Muscular Skeletal/Dermatologic

Nonspecific or Unknown Body System

Select ONE Adverse event from listing in applicable category

Subject Study ID | 201202 | | | | - | | | | Site# | | | |

DATE OF REOPERATION/ REMOVAL/ EXPLANT ___ ___ / ___ ___ ___ / ___ ___ ___ ___
D D M M M Y Y Y Y

SURGERY OCCURRED AT INVESTIGATIONAL CENTER: ☐ YES ☐ NO

TYPE OF PROCEDURE PERFORMED:

☐ EXPLANT
☐ VALVE IN VALVE REPLACEMENT:
MANUFACTURER and MODEL:_____ SIZE (MM): _____
☐ OTHER, SPECIFY: _____

EXPLANT PROCEDURE ☐ NAP

WHAT WAS THE SURGICAL APPROACH USED FOR THE EXPLANT PROCEDURE?

☐ FULL STERNOTOMY ☐ RIGHT THORACOTOMY
☐ MINI UPPER STERNOTOMY ☐ NOT AVAILABLE

WHAT TYPE OF AORTOTOMY WAS PERFORMED? _____

WHAT WAS REMOVED? ☐ NOT AVAILABLE

☐ BIOPROSTHESIS LEAFLETS
☐ BIOPROSTHESIS SEWING RING

WAS A ROOT ABSCESS PRESENT AT REOPERATION? ☐ NO ☐YES

EASE OF STUDY VALVE EXPLANT: ☐1 ☐2 ☐3 ☐4 ☐5 ☐N/A (5 is the easiest/best)

WAS A REPLACEMENT VALVE IMPLANTED?

☐ NO ☐YES MANUFACTURER and MODEL:_____ SIZE (MM): _____

DEVICE GROSS EVALUATION (APPEARANCE OF VALVE PRIOR TO OR IMMEDIATELY FOLLOWING EXPLANT)
ANSWER EACH YES OR NO

YES	NO	
☐	☐	THROMBUS
☐	☐	VEGETATION
☐	☐	SUTURE INTERFERENCE
☐	☐	CALCIFICATION
☐	☐	FIBROSIS
☐	☐	DEHISCENCE
☐	☐	OTHER, SPECIFY: _____

DID EXCISION OF STUDY VALVE REQUIRE OR RESULT IN STRUCTURAL CHANGES? ☐ NOT AVAILABLE

☐ NO ☐YES, SPECIFY: _____

WAS EXPLANTED STUDY VALVE RETURNED? ☐ NO ☐YES, RGA#: _____

_____ DATE SIGNED ___ ___ ___ ___ ___ ___ ___ ___
SIGNATURE D D M M M Y Y Y Y

Subject Study ID | 201202 | | | | - | | | | Site# | | | |

A. DATE OF STUDY EXIT

__ __ / __ __ __ / __ __ __ __
D D M M M Y Y Y Y

B. REASON FOR EXIT (SELECT ONE)

☐ **1. SUBJECT COMPLETED PROTOCOL REQUIRED FOLLOW UPS**

☐ **2. SUBJECT DID NOT RECEIVE STUDY VALVE DURING THE INDEX PROCEDURE AND COMPLETED THE PROTOCOL REQUIRED FOLLOW-UP PERIOD**

☐ **3. STUDY VALVE EXPLANTED AND SUBJECT COMPLETED THE PROTOCOL REQUIRED FOLLOW-UP PERIOD**

☐ **4. SUBJECT MET AN EXCLUSION CRITERION AFTER STUDY ENROLLMENT**

☐ **5. SUBJECT VOLUNTARY WITHDREW OR SUBJECT WITHDRAWN BY INVESTIGATOR**

☐ a. POST STUDY PROCEDURE BUT PRIOR TO DISCHARGE

☐ b. POST DISCHARGE FROM THE HOSPITAL

PLEASE INDICATE THE REASON FOR WITHDRAWAL:

_____

☐ **6. SUBJECT LOST TO FOLLOW-UP** (SUBJECT MISSED 2 SEQUENTIAL FOLLOW-UP VISITS)

☐ **7. DEATH**

A. DATE OF DEATH _ _ / _ _ _ / _ _ _ _ (DD/MMM/YYYY)

B. DID THE SUBJECT DIE INTRAOPERATIVELY DURING THE STUDY PROCEDURE? ☐ YES ☐ NO

C. DID THE SUBJECT DIE PRIOR TO DISCHARGE FROM THE HOSPITAL AFTER THE STUDY PROCEDURE? ☐ YES ☐ NO

D. CAUSE OF DEATH:_____

DATE REPORTED TO SPONSOR: _____ (DD/MMM/YYYY)

PLEASE PROVIDE THE FOLLOWING INFORMATION ABOUT THE SUBJECT'S HOSPITALIZATION AFTER THE STUDY VALVE PROCEDURE:

DURATION AND TIME IN THE INTENSIVE CARE UNIT (ICU) _____DAYS AND _____HOURS

DURATION AND TIME IN THE INTERMEDIATE CARE/ HIGH DEPENDENCY UNIT

_____DAYS AND _____HOURS

DURATION AND TIME IN THE GENERAL WARD _____DAYS AND _____HOURS

DATE OF AUTOPSY:_____(DD/MMM/YYYY) ☐ NOT APPLICABLE

WAS A STUDY VALVE REMOVED AT AUTOPSY? ☐ YES ☐ NO
(IF YES, FILL OUT REOP_EXP FORM)

☐ **8. OTHER REASON,** SPECIFY: _____

_____ DATE SIGNED | | | | | | | | |
SIGNATURE D D M M M Y Y Y Y

Subject Study ID **201202** | | | | - | | | | Site# | | | |

1. **DATE OF DEVIATION:** __ __/__ __ __ / __ __ __ __
   D D M M M Y Y Y Y

2. **PLEASE SELECT PROTOCOL DEVIATION CODE** (PROTOCOL DEVIATION CODE LIST)

   EVENT CODE: _____

   IF MISSED VISIT, SPECIFY:

   1st ATTEMPTED CONTACT _____(DD/MMM/YYYY), TIME (HH:MM)

   2nd ATTEMPTED CONTACT _____(DD/MMM/YYYY), TIME (HH:MM)

   3rd ATTEMPTED CONTACT _____(DD/MMM/YYYY), TIME (HH:MM)

   CAN YOU CONFIRM THROUGH ANY SOURCES THAT THE SUBJECT IS ALIVE? ☐ No ☐ Yes

   IF OTHER DEVIATION, SPECIFY:

   _____

3. **REASON:**

   ☐ NOT ORDERED BY PHYSICIAN

   ☐ OVERSIGHT

   ☐ PATIENT NOT AVAILABLE

   ☐ PATIENT TOO SICK TO HAVE TEST

   ☐ OTHER, SPECIFY:

_____

4. **CORRECTIVE ACTION:**

   ☐ STUDY STAFF RE-TRAINED

   ☐ OTHER, SPECIFY:

   _____

_____ DATE SIGNED | | | | | | | | |
SIGNATURE D D M M M Y Y Y Y

ECHO CORE LAB TRACKING FORM

Date ECHO received by core lab | | / | | / | | (DD/MMM/YYYY)

Date of readability assessment | | / | | / | | (DD/MMM/YYYY)

Please indicated whether or not the images were readable (check one):

☐ Readable

☐ Partially readable

☐ Not readable

Was a request sent to the site to resend the images?

☐ No ☐ Yes

Date of resend request: | | / | | / | | (DD/MMM/YYYY)

Was the readability issue resolved?

☐ No ☐ Yes

Date readability issue resolved: | | / | | / | | (DD/MMM/YYYY)

Was the ECHO assessed by the core lab?

☐ No ☐ Yes

ECHO CORE LAB EVALUATION

Physical Assessment

Subject weight _____ ☐ kg ☐ lb

Body Surface Are (BSA) _____ m^2 ☐ Not evaluable

Heart rate _____ bpm

Blood pressure _____ / _____ mmHg

Does the ECHO indicate the subject has the following cardiac rhythm/conducting system disturbances?

No	Yes	Indeterminate	
☐	☐	☐	Normal sinus rhythm
☐	☐	☐	Atrial fibrillation
☐	☐	☐	Atrial flutter
☐	☐	☐	Ventricular tachycardia
☐	☐	☐	Ventricular fibrillation
☐	☐	☐	AV Block
			Please indicate the degree: ☐ 1st ☐ 2nd ☐ 3rd ☐ Unknown
☐	☐	☐	Bundle branch block
			Please specify the location: ☐ Left ☐ Right ☐ Not evaluable
☐	☐	☐	Paced rhythm
			Please specify the location: ☐ Atrial ☐ Ventricular ☐ Atrioventricular

Valve Assessment: Stenosis

Please indicate the level of aortic stenosis (check one):

☐ None

☐ Mild

☐ Moderate

☐ Severe

☐ Not evaluable

Is there mitral stenosis?

☐ Yes ☐ No

If Yes,

☐ Mild

☐ Moderate

☐ Severe

☐ Not evaluable

Etiology of mitral stenosis:

☐ Calcific

☐ Rheumatic

☐ Other: Specify _____

☐ Indeterminate

LV Structure/Regional Function

Please indicate if any of the following abnormalities were observed:

No	Yes	
☐	☐	LV aneurysm
		Please specify the location: _____
☐	☐	Wall motion abnormality
		Please specify: _____
☐	☐	Cavity dilation

☐ ☐ Apical and/or left atrial thrombi

Please specify: _____

☐ ☐ Other abnormality

Global LV Structure/Function

What method of calculation was used for LV function assessment (check one)?

☐ Biplane

☐ Single

☐ Quinones

☐ Visual

LVEDV		ml	☐ Not evaluable
LVESV		ml	☐ Not evaluable
LVEF		%	☐ Not evaluable

LV Dimension

Septal thickness (end-diastolic)		cm	☐ Not evaluable
Posterior wall thickness (end-diastolic)		cm	☐ Not evaluable
LV end-diastolic dimension		cm	☐ Not evaluable
LV end-systolic dimension		cm	☐ Not evaluable
LV mass		g	☐ Not evaluable
LV mass index (BSA Corrected LV Mass)		g/m^2	☐ Not evaluable
Left Atrium (LA)		mm	☐ Not evaluable

Aortic Dimensions

LVOT diameter		cm	☐ Not evaluable
Aortic annulus		cm	☐ Not evaluable
Aortic root diameter		cm	☐ Not evaluable

STJ diameter _____ cm ☐ Not evaluable

Valve Assessment: Measurements

Please fill out this section for the Trial arm position

V_{peak}		m/sec	☐ Not evaluable
TVI		cm	☐ Not evaluable
Peak gradient (by continuous wave)		mmHg	☐ Not evaluable
Mean gradient (by continuous wave)		mmHg	☐ Not evaluable
TVI (LVOT)		cm	☐ Not evaluable
Maximum V(LVOT)		m/sec	☐ Not evaluable
Mean V(LVOT)		m/sec	☐ Not evaluable
Stroke volume *[LVOT derived for aortic position; across mitral valve for mitral position]*		ml	☐ Not evaluable
Transvalvular flow	_____	mL/s	☐ Not evaluable
Cardiac output (LVOT derived)	_____	L/min	☐ Not evaluable
Cardiac index	_____	$L/min/m^2$	☐ Not evaluable
EOA (continuity equation)	_____	cm^2	☐ Not evaluable
EOA index	_____	cm^2/m^2	☐ Not evaluable
Performance index	_____	cm^2/cm^2	☐ Not evaluable

Valve Assessment: Regurgitation

Please fill out this section for the Trial arm position

Please identify all the methods of calculation used:

No	Yes	
☐	☐	Color doppler
☐	☐	Regurgitant fraction
☐	☐	Proximal convergent flow

☐ ☐ Continuous wave Doppler (pressure half-time, only applicable to aortic regurgitation)

☐ ☐ Aortic/pulmonary flow reversal

Please indicate the paravalvular leak severity:

☐ 0 None

☐ +1 Trivial/Trace

☐ +2 Mild

☐ +3 Moderate

☐ +4 Severe

☐ Not evaluable

☐ Not applicable

If the paravalvular leak severity is +2, +3, or +4, please indicate the following:

Number of jets: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ Other, specify:

Please indicate the location of the jets:

Please indicate the image view of the jets: ☐ PLAX ☐ PSAX ☐ A5C ☐ A3C

Please indicate the transvalvular leak severity:

☐ 0 None

☐ +1 Trivial/Trace

☐ +2 Mild

☐ +3 Moderate

☐ +4 Severe

☐ Not evaluable

Please indicate the total regurgitation severity:

☐ 0 None

☐ +1 Trivial/Trace

☐ +2 Mild

☐ +3 Moderate

☐ +4 Severe

☐ Not evaluable

Primary mechanism of mitral valve regurgitation (Note: Only applicable if subject is in the mitral arm at baseline visit)

☐ Type I – Normal Leaflet Motion

☐ Type II – Leaflet Prolapse

☐ Type IIIa – Restricted leaflet opening

☐ Type IIIb – Restricted leaflet closure

☐ Not evaluable

☐ Not applicable

Valve Morphology

Please indicate the degree of calcification:

☐ Not evaluable

☐ None

☐ Mild

☐ Moderate

☐ Heavy

Please indicate the degree of annular calcification (only applicable to mitral arm):

☐ Not applicable

☐ Not evaluable

☐ None

☐ Mild

☐ Moderate

☐ Heavy

Please indicate whether the following morphologies were observed:

No	Yes	
☐	☐	Cusp perforation
☐	☐	Pannus formation
☐	☐	Thrombus
☐	☐	Vegetation
☐	☐	Ring abscess
☐	☐	Pseudoaneurysm

Non-Trial Arm Valve Assessment

Please indicate the level of tricuspid valve regurgitation

☐ 0 None

☐ +1 Trivial/Trace

☐ +2 Mild

☐ +3 Moderate

☐ +4 Severe

☐ Not evaluable

Please indicate the level of mitral valve regurgitation
[Note: Select 'Not applicable' if subject is in the Mitral Trial arm]

☐ 0 None

☐ +1 Trivial/Trace

☐ +2 Mild

☐ +3 Moderate

☐ +4 Severe

☐ Not evaluable

☐ Not applicable

Please indicate the level of aortic valve regurgitation
[Note: Select 'Not applicable' if subject is in the Aortic Trial arm]

☐ 0 None

☐ +1 Trivial/Trace

☐ +2 Mild

☐ +3 Moderate

☐ +4 Severe

☐ Not evaluable

☐ Not applicable

Pericardial effusion

Please indicate the level of pericardial effusion:

☐ None

☐ Small

☐ Moderate

☐ Large

☐ Tamponade

☐ Not evaluable

☐ Other, specify: _____

RV Function

Please indicate the overall assessment of the right ventricle

☐ Normal

☐ Abnormal

ECHO Quality

Please indicate the overall quality of the ECHOs

☐ Good

☐ Fair

☐ Poor

☐ Inadequate

COMMENTS:

ATTACHMENT E – CORE LABORATORY PROCEDURE MANUAL

Core Laboratory Procedure Manual *(For Model 11000A)*

*Prospe**C**tive, n**O**n-rando**M**ized, **M**ultic**EN**ter **C**linical Evaluation of the **E**dwards Pericardial Aortic & Mitral Bioprostheses (Models 11000A & 11000M) with a New Tissue Treatment Platform*

(COMMENCE TRIAL)

Clinical Protocol Number 2012-02

Revision E

Table of Contents

Contents

1. Introduction and General Objectives

Echocardiographic measures of aortic valve function, mitral valve function and left ventricular size and function are used as markers of success in this trial. The echocardiogram will be performed at specified time points. The majority of the echocardiograms will be transthoracic echocardiograms and this document focuses on this technique. The details of the image planes and the measurement conventions are described below.

2. Echo Timeline

Each subject enrolled in the trial will have a completed echo at all of the following time points:

Follow-up Visit	Visit Window
Screening	Day -60 to Day 0
Operative (**TEE**)	Within 1 hr from cross clamp removal
Discharge	Prior to POD +10, or prior to Discharge, whichever is earlier
POD 105	-15/+10 days
POD 390	-25/+45 days
POD 730	-25/+45 days
POD 1095	-25/+45 days
POD 1460	-25/+45 days
POD 1825	-25/+45 days
POD 2190 (6 yr)*	-55/+75 days
POD 2555 (7 yr)*	-55/+75 days
POD 2920 (8 yr)*	-55/+75 days
POD 3285 (9 yr)*	-55/+75 days
POD 3650 (10yr)*	-55/+75 days

* Only required for subjects who have consented to continued follow-up with the Model 11000A valve at the top 3 enrolling sites.

All echocardiograms should be full transthoracic echocardiograms (TTE) except at the operative interval, where a full transesophageal echocardiogram (TEE) should be performed. A TEE may also be accepted for the baseline/screening echocardiogram.

If applicable, always label the echo (or CD) with Subject ID, Visit Interval, and Exam Date and attach the Echo (Site) worksheet with vitals/ heart rhythm information. Please check to see that the demographic information on the images matches the data sheet.

3. Examination Protocol – Cardiac Echo-Doppler

OBJECTIVES:

- The primary objective of the initial echo-Doppler examination is to establish baseline cardiac anatomy and function with an emphasis on the aortic valve, aortic root and left ventricular size and function
- The primary goals of the follow-up post-implantation studies are to reassess the aortic valve prosthesis (structure and function) and to determine the impact of the implantation on the parameters evaluated.
- Complete Echo-Doppler examinations are required at the time points specified in the table above.
- Two-dimensional ultrasound imaging systems with pulsed, continuous wave and color Doppler capability, and permanent recording capabilities are required.
- **The only accepted storage format is DICOM standard digital.**
- You should have transducers with both fundamental and harmonic capability with frequency ranges that are suitable for most adult subjects (approximately 2 to 7 mHz).

EXAMINATION PREPARATION, POSITIONING, AND GENERAL PROCEDURES:

- A qualified physician or sonographer must perform all ultrasound exams. If possible, participating sites should attempt to utilize the same person as well as the same machine for image acquisition throughout the trial.
- Prior to starting the study, the physician/sonographer should provide the subject with an overview of the study (duration, general procedure etc).
- Subjects will typically be studied while they are in the left lateral decubitus position although occasionally the best images will be obtained with the subject supine.
- EKG leads will be applied and the EKG control setting of the machine optimized to ensure a high quality EKG with adequate amplitude QRS complex for reliable digital capture (lead II equivalent preferred).
- All views will be acquired with 2 captures OF EACH VIEW as follows:
  - Sinus rhythm (up to 90 bpm): 3 beat capture
  - Sinus rhythm (more than 90 bpm): 5 beat capture
  - Frequent atrial or ventricular ectopy: 3 second capture
  - Atrial fibrillation or flutter, paced rhythm: 5 second capture
- It is essential that the view be optimized and stabilized before recording. Images are typically acquired during quiet respiration. Breath-holding during recording is not required unless necessary to ensure a stable high quality image.
- The spatial resolution of the images should be optimized using the highest frequencies capable of providing adequate penetration. For each view, the gain, compression and focus should be optimized so that the best echocardiographic image of the endocardial borders is obtained.
- Use echo contrast if available for images with suboptimal endocardial definition

- The sweep speed for all spectral Doppler and M-mode recordings should be 100 mm/sec. NOTE: at least 3 consecutive sinus beats and at least 5 consecutive "irregular rhythm" beats must be captured, so adjust the number of captures accordingly.
- As defined in the ASE Guidelines for the Quantification of Native Valve Regurgitation, Nyquist settings for color Doppler assessment of the cardiac valves should be 50-60 cm/sec.
- We encourage you to perform measurements as needed for clinical feedback to treating physicians. If you do perform on-line measurements, please do not obscure the flow profiles of subsequent beats. We suggest storing BOTH measured and unmeasured Doppler spectra and images.

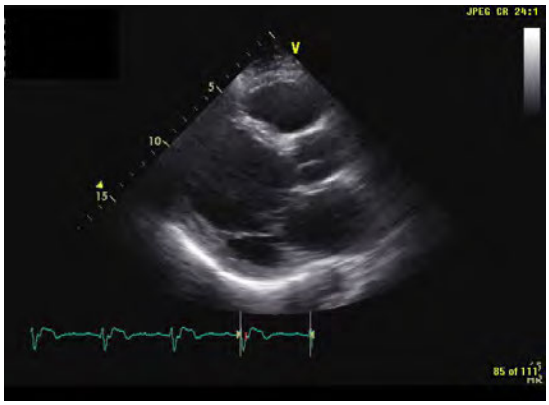
- Once the data storage/file save operation is complete, transmit the data to the Core Lab, utilizing the instruction documentation provided in the AG Mednet Desktop Agent.
    - De-identify the images through the AG Mednet while uploading data. Enter the subject information as specified on the Echo Tracking Form. Importantly, the height and weight will have to be entered at every follow-up interval. Please measure and note the blood pressure on the subject ID screen or as an annotation on one or more images.

EXAMINATION SEQUENCE:

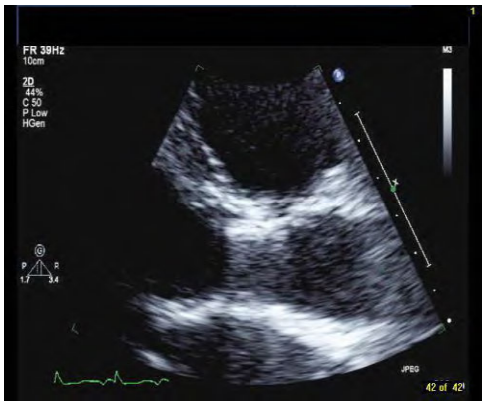
I. **Parasternal Long Axis of LV, LVOT and AV**

- 2D (Image A below)
- Color Doppler of MR
- Color Doppler of LVOT and aortic valve (AV) for aortic insufficiency
- Magnified views of LVOT and aortic valve – to identify the true LVOT dimension, AV annulus and stent diameter (Image B below)
- High parasternal view to see ascending aorta
- Off-axis views to search for aortic paravalvular leak
- Obtain an RV inflow view
- Color flow Doppler of triscuspid valve
- Pulse wave Doppler of inflow 1-2cm below the valve
- Continuous wave Doppler of TV

- Obtain RV outflow to include bifurcation if possible
- Color flow Doppler of PA
- Pulse wave Doppler of the pulmonary valve 1-2 cm below the valve in the outflow tract
- Continuous wave Doppler of PA



A.



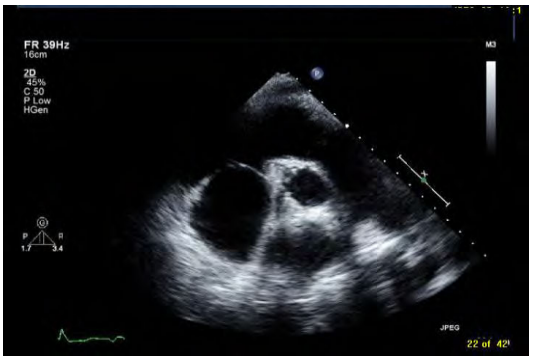
B.

II. **Parasternal Short axis at LV level**

- 2D should be obtained at 3 levels: apex, mid-papillary muscle and base
- Color Doppler of MR from the basal view is also requested

III. Parasternal Short axis at aortic valve level

- 2D
- Color Doppler of aortic valve including sewing ring of prosthesis to search for paravalvular leak
- Color Doppler of TR is optional in this view

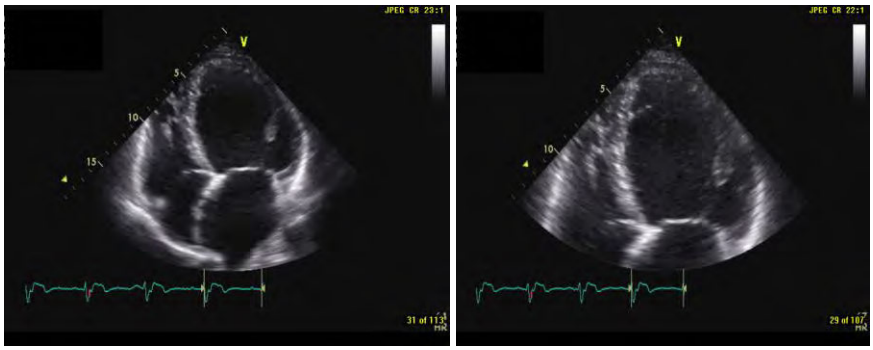


IV. Apical 4 chamber

- 2D optimizing LV endocardial borders: Need to see all aspects of the lateral wall, septum, and apex
- Show a loop with decreased depth such that LV occupies most of the imaging sector ensuring all walls are visualized
- Color Doppler of MR showing entire left atrium (to allow jet dimension/LA measurement)
- If there is more than mild MR, provide components for PISA calculation
  - CW of MR jet
  - Zoomed PISA display (baseline shift down to optimize hemispherical PISA shell)
  - The aliasing velocity of color scale should be shifted down or towards MR jet to around 40cm/sec

- If possible, provide split screen (color suppress) images (i.e. one side with color, one without)

- Color Doppler of TR with CW

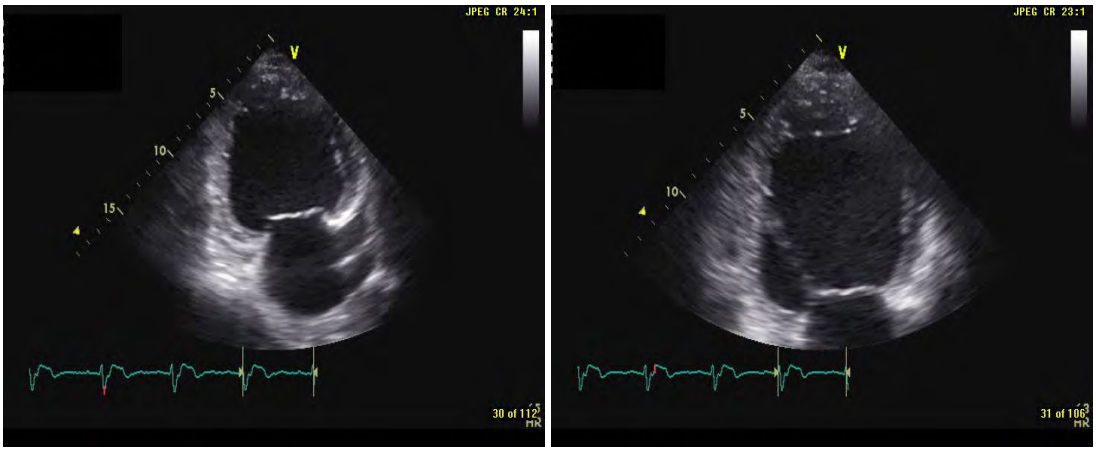


V. Apical 5 chamber view

- Pulse wave Doppler of LVOT **(to avoid the region of flow acceleration - sample volume should be positioned at valve level and then moved apically until valve noise or "clicks" are no longer detected and then recorded for the baseline study)**
- **For post-implantation studies, it is imperative that the sample volume be placed proximal to the valve frame AND at a second position within the valve frame but proximal to the valve cusps. Studies in which there are no clips with the sample volume proximal to the valve frame will be considered INADEQUATE.**
- Note: record a full screen 2D image showing the pulse wave sample position (either as moving image or still frame) as well as the Pulse Wave Spectral Doppler for each position. It is very difficult to establish the sample volume position from the small image that is available when image and spectral display are provided simultaneously.
- Color Doppler of LVOT and aortic valve for AI (use off axis views to ensure that all AI jets are demonstrated)
- Continuous wave and pulse wave Doppler through the aortic valve
- Continuous wave Doppler through the aortic valve
- Pulse Wave Doppler the left ventricular outflow tract

VI. Apical 2 chamber

- 2D optimizing LV endocardial borders: Need to see all aspects of the anterior wall, inferior wall, and apex
- Show a loop with decreased depth such that LV occupies most of the imaging sector ensuring all walls are visualized
- Color Doppler of MR

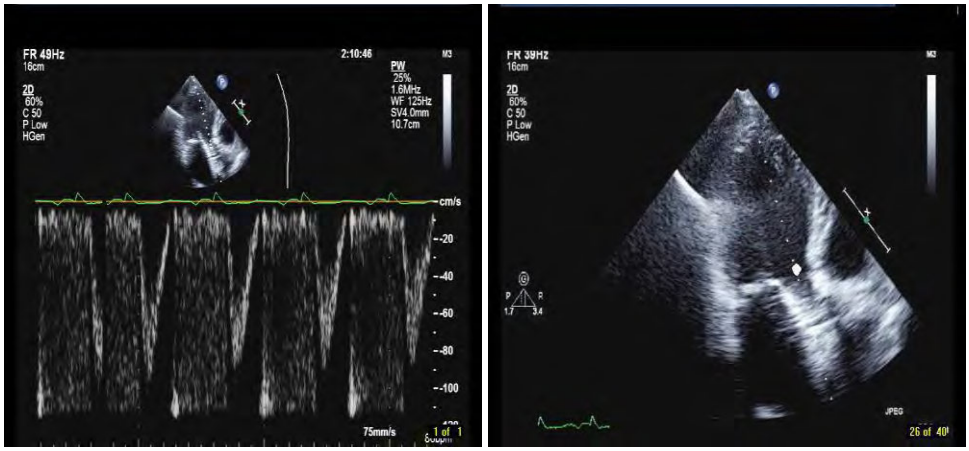


A. B.

** Image A shows the traditional 2 chamber while image B shows the 2 chamber with decreased depth*

VII. Apical long axis view (also known as 3 chamber view)

- Color Doppler of MR
- Color Doppler of LVOT and aortic valve for AI (use off axis views to ensure that all AI jets are demonstrated)
- Pulse Wave Doppler just **apical to the valve frame** as specified in apical 5 chamber view
- Note: record a full screen 2D image showing the pulsed wave sample position (either as moving image or still frame) as well as the Pulse Wave Spectral Doppler for each position
- Continuous Wave Doppler through the aortic valve



A. B.

VIII. Right Parasternal view

- Continuous Wave Doppler through the aortic valve (Note: this view is particularly useful if you notice an anteriorly-directed transaortic jet from parasternal views)

IX. Suprasternal Notch view

- Pulsed Doppler of the descending thoracic aorta from the suprasternal notch should be obtained to assess for reversal of flow if significant (moderate or greater) aortic insufficiency is present **(Note: sample volume is placed in the descending thoracic aorta below the take off of the subclavian artery).**
- Continuous wave Doppler interrogation of the transaortic valvular flow should also be obtained using the pedoff transducer

X. Specific Comments on Imaging Planes

A. Parasternal long axis view is recorded with the transducer in the third or fourth intercostal space immediately to the left of the sternum. The transducer should be angled so that the aortic valve, mitral valve and left ventricle are in their long axis.

IMAGING TIP 1: PARASTERNAL LONG AXIS VIEW

It is important that the parasternal long axis view displays the true long axis of the ventricle with the left ventricle lying horizontally on the image. If it is impossible to obtain a single view which optimally displays the long axis of the aortic valve and aortic root as well as the long axis of the left ventricle, record 2 separate views. It is unacceptable to record an off-axis view in which the apex "points up" on the screen. If this type of image is obtained try moving the transducer up 1-2 intercostal spaces or having the subject take a breath in. Sometimes having the subject move to a more lateral decubitus position will help as well.

IMAGING TIP 2: PARASTERNAL LONG AXIS VIEW

Measurement of the left ventricular outflow tract and aortic annulus is a key component of the study. In pre-device imaging, it is important to note that the largest annulus may not be in a plane with valve opening centered in the aorta.

B. Parasternal short axis view is obtained by angling the probe 90° with respect to the parasternal long axis of the LV. The goal of this view is to obtain information about the aortic valve as well as the LV.

IMAGING TIP 3: PARASTERNAL SHORT AXIS VIEW

This is an essential view post-op to completely assess aortic regurgitation. This may be the only view in which prosthetic valve medial or lateral aortic regurgitant jets are imaged. Imaging at the level of as well as just below the leaflets may allow you to better image these jets.

C. **Apical four-chamber** view provides considerable information including the relative sizes of the right and left ventricles and the regional function of the LV. The four chamber view is defined as a view which maximizes the LV long axis and the tricuspid and mitral annular dimensions. In this view, the full excursion of the mitral and tricuspid valves should be seen. The complete endocardial border of the LV will be traced for chamber volume assessment (method of discs) so all aspects including the apex should be visualized. In the apical four chamber view, color Doppler of mitral and tricuspid regurgitation should be recorded. The four chamber view should visualize the lateral, septal and apical walls.

D. **Apical two-chamber** view should be obtained for the goal of assessment of LV size and function. The complete endocardial border of the LV will be traced for chamber volume assessment (method of discs) so all aspects including the apex should be visualized. The degree of MR by color Doppler will also be assessed. The two chamber view should visualize the anterior, inferior and apical walls.

IMAGING TIP 4: APICAL 4 and 2 CHAMBER VIEWS

Because we will measure volumes from the apical views as an important end-point of the study, please try to avoid apical foreshortening. If the view appears to be foreshortened, please bring the transducer down one intercostal space and have the subject take a breath in (particularly for the apical two-chamber view). Sometimes this will bring out a better (not foreshortened) view.

E. **Apical 5 chamber and 3 chamber** views are obtained to provide detailed information about the aortic valve color, spectral and continuous wave Doppler.

IMAGING TIP 5: APICAL 5 and 3 CHAMBER VIEWS

Both these views are essential in imaging post-device aortic regurgitant jets. Because we will be measuring jet vena contracta and jet length, a Res/Zoom view which includes imaging of the entire jet would be helpful. In addition, the 3Ch view may be used in the biplane Simpson's calculation of LV volume when the 2Ch view is inadequate. Thus, careful attention to endocardial definition is important.

XI. Abbreviations

2D=Two-dimensional
AI =Aortic Insufficiency
AR=Aortic Regurgitation
AV=Aortic Valve
AVA=Aortic valve area
BSA=Body Surface Area
CO=Cardiac Output
CSA=Cross sectional area
ED=End diastole
EF=Ejection fraction
ES=End systole
HR =Heart rate
LA=Left atrium
LV=Left Ventricle
LVED=Left ventricular end diastolic volume
LVEF=Left ventricular ejection fraction
LVES=Left ventricular end systolic volume
LVOT=Left ventricular outflow tract
MR=Mitral Regurgitation
MV=Mitral Valve
PI=Performance Index
PW=Pulse wave
SV=Stroke Volume
TR=Tricuspid Regurgitation
TVI or VTI=Time Velocity Integral

4. Site Echocardiographer Checklist

Labeling and Demographics:

Subject Study ID: _____

Visit: Baseline Operative Discharge POD 105
POD 390 2 yr 3yr 4yr 5yr
6 yr 7 yr 8 yr 9 yr 10 yr
Interim (Specify Reason): _____

Exam Date __ __/__ __ __/__ __ (Day/Month/Year)
Height: _____ cm
Weight: _____ kg
Heart Rate: _____ bpm
Rhythm: _____
Blood Pressure (mmHg):
Systolic_____
Diastolic_____

I. Parasternal Long Axis of LV, LVOT, Aortic Valve views
- ☐ 2D
- ☐ Color Doppler of MR
- ☐ Color Doppler of LVOT/aortic valve for AR
- ☐ Magnified views of LVOT and aortic valve
- ☐ High Parasternal View (ascending aorta)
- ☐ Off-axis views to search for paravalvular AR

II. Parasternal Short axis at LV level
- ☐ LV apex,
- ☐ LV mid-papillary muscle
- ☐ LV base
- ☐ Color Doppler of MR (basal view—optional)

III. Parasternal Short axis at AV level
- ☐ 2D
- ☐ Color Doppler of aortic valve
- ☐ Color Doppler of TR (optional)

IV. Apical 4 chamber
- ☐ 2D optimizing LV endocardial borders
- ☐ LV with decreased depth
- ☐ Color Doppler of MR
- ☐ Color Doppler of TR (with CW)
- ☐ PISA if more than mild MR

V. Apical 5 chamber view

- ☐ Pulsed Wave Doppler of LVOT (multiple levels)
- ☐ Continuous wave Doppler through the AV
- ☐ Color Doppler of LVOT and aortic valve

VI. Apical 2 chamber

- ☐ 2D optimizing LV endocardial borders
- ☐ LV with decreased depth
- ☐ Color Doppler of MR

VII. Apical long axis (3 chamber) view

- ☐ 2 D optimizing LV endocardial borders
- ☐ LV with decreased depth
- ☐ Pulsed Wave Doppler at the LVOT
- ☐ Continuous Wave Doppler through AV
- ☐ Color Doppler of LVOT and aortic valve for AI
- ☐ Color Doppler of MR

VIII. Right Parasternal view

- ☐ Continuous Wave Doppler through AV

IX. Suprasternal Notch view

- ☐ Pulsed Wave Doppler of the descending thoracic aorta for AI
- ☐ Continuous Wave Doppler through AV

5. Core Lab Echo Tracking Form

An Echo Tracking Form will be completed for each subject including the following information, and will be submitted along with the echo data via AG Mednet (vendor providing digital transfer of echo data) to the Core Lab:

1. Follow-up interval
2. Exam transfer date
3. Exam date
4. Subject number
5. Site number
6. Echo type: TTE/ TEE
7. Heart rate (bpm)
8. Cardiac rhythm
9. Site comments
10. Name and email of person completing form
11. Scan date
12. Date completed
13. DICOM scan date
14. Echo scanner manufacturer name and model
15. Subject height (cm) and weight (kg)

6. Site Data Collection/ Entry into Oracle EDC (Echo Tracking Form)

Each echocardiogram should also be read by the sites and data should be entered on the appropriate case report form (CRF). Data to be reported in addition to what is requested in the Echo Tracking Form include the following measurements:

- Subject blood pressure (systolic and diastolic)

- LVOT assessment:
  - Peak velocity
  - Peak gradient
  - Mean gradient
  - VTI

- Aortic valve assessment:
  - Peak velocity
  - Peak gradient
  - Mean gradient
  - VTI
  - Annulus size (cm)
  - AV area (cm^2)

- Aortic regurgitation severity
  - 0 None
  - +1 Trivial/Trace

- +2 Mild
- +3 Moderate
- +4 Severe
- Indeterminate

- Mitral regurgitation severity
  - 0 None
  - +1 Trivial/Trace
  - +2 Mild
  - +3 Moderate
  - +4 Severe
  - Indeterminate

- LVEF
  - Range of LVEF
  - Method used to determine LVEF (single plane or biplane)

- Severity of paravalvular leak (PVL)
  - 0 None
  - +1 Trivial/Trace
  - +2 Mild
  - +3 Moderate
  - +4 Severe
  - Indeterminate

- Assessment of RV function
  - Normal
  - Mildly reduced
  - Severely reduced
  - Indeterminate

- Method of delivery of echocardiographs to Core Lab
  - Images uploaded, FedEx, UPS, DHL, Other
  - Tracking number

7. Shipping & Contact Information

A copy of all documents and data must be kept at your site. Documents and CD's must be labeled with the trial protocol number (Protocol # 2012-02), the site ID, subject ID, subject initials, exam date, and exam interval.

Though all data is preferred to be uploaded digitally via AG Mednet, if shipping CDs, please send us an e-mail at when you ship your package. Upon its receipt, an official e-mail notification will be sent from the Core Lab to your site coordinator. Please confirm that the e-mail notification correlates with your shipping records. You should contact the Core Lab immediately with any discrepancies or if you have shipped a study but you have not received an e-mail notification within 2 business days.

Please do not hesitate to contact us with any questions. For non-urgent communications, e-mail is typically the best means.

For echo-related urgent questions, please call

are looking forward to being your partners in this important clinical trial.

Core Laboratory Procedure Manual ***(For Model 11000M)***

ProspeCtive, nOn-randoMized, MulticENter Clinical evaluation of the Edwards Pericardial Aortic & Mitral Bioprostheses (Models 11000A & 11000M) with a new tissue treatment platform (COMMENCE TRIAL)

Clinical Protocol Number 2012-02

Revision F

Table of Contents

Contents

1. Introduction and General Objectives

Echocardiographic measures of aortic valve function, mitral valve function and left ventricular size and function are used as markers of success in this trial. The echocardiogram will be performed at specified time points. The majority of the echocardiograms will be transthoracic echocardiograms and this document focuses on this technique. The details of the image planes and the measurement conventions are described below.

2. Echo Timeline

Each subject enrolled in the trial will have a completed echo at all of the following time points:

Follow-up Visit	Visit Window
Screening	Day -60 to Day 0
Operative (**TEE**)	Within 1 hr from cross clamp removal
Discharge	Prior to POD +10, or prior to Discharge, whichever is earlier
POD 105	-15/+10 days
POD 390	-25/+45 days
POD 730	-25/+45 days
POD 1095	-25/+45 days
POD 1460	-25/+45 days
POD 1825	-25/+45 days
POD 2190 (6 yr)*	-55/+75 days
POD 2555 (7 yr)*	-55/+75 days
POD 2920 (8 yr)*	-55/+75 days
POD 3285 (9 yr)*	-55/+75 days
POD 3650 (10yr)*	-55/+75 days

* Only required for subjects who have consented to continued follow-up with the Model 11000M valve at the 3 enrolling sites.

All echocardiograms should be full transthoracic echocardiograms (TTE) except at the operative interval, where a full transesophageal echocardiogram (TEE) should be performed. A TEE may also be accepted for the baseline/screening echocardiogram.

If applicable, always label the echo (or CD) with Subject ID, Visit Interval, and Exam Date and attach the Echo (Site) worksheet with vitals/ heart rhythm information. Please check to see that the demographic information on the images matches the data sheet.

3. Examination Protocol – Cardiac Echo-Doppler

OBJECTIVES:

- The primary objective of the initial echo-Doppler examination is to establish baseline cardiac anatomy and function with an emphasis on the mitral valve and left ventricular size and function
- The primary goals of the follow-up post-implantation studies are to reassess the mitral valve prosthesis (structure and function) and to determine the impact of the implant on the parameters evaluated.
- Complete Echo-Doppler examinations are required at the time points specified in the table above.
- Two-dimensional ultrasound imaging systems with pulsed, continuous wave and color Doppler capability, and permanent recording capabilities are required.
- **The only accepted storage format is DICOM standard digital.**
- You should have transducers with both fundamental and harmonic capability with frequency ranges that are suitable for most adult subjects (approximately 2 to 7 mHz).

EXAMINATION PREPARATION, POSITIONING, AND GENERAL PROCEDURES:

- A qualified physician or sonographer must perform all ultrasound exams. If possible, participating sites should attempt to utilize the same person as well as the same machine for image acquisition throughout the trial.
- Prior to starting the study, the physician/sonographer should provide the subject with an overview of the study (duration, general procedure etc).
- Subjects will typically be studied while they are in the left lateral decubitus position although occasionally the best images will be obtained with the subject supine.
- EKG leads will be applied and the EKG control setting of the machine optimized to ensure a high quality EKG with adequate amplitude QRS complex for reliable digital capture (lead II equivalent preferred).
- All views will be acquired with 2 captures OF EACH VIEW as follows:
  - Sinus rhythm (up to 90 bpm): 3 beat capture
  - Sinus rhythm (greater than 90 bpm): 5 beat capture
  - Frequent atrial or ventricular ectopy: 3 second capture
  - Atrial fibrillation or flutter, paced rhythm: 5 second capture
- It is essential that the view be optimized and stabilized before recording. Images are typically acquired during quiet respiration. Breath-holding during recording is not required unless necessary to ensure a stable high quality image.

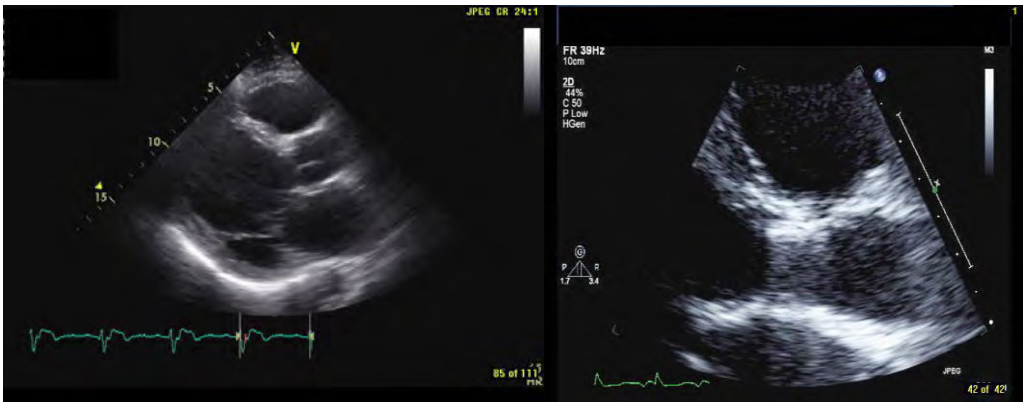
- The spatial resolution of the images should be optimized using the highest frequencies capable of providing adequate penetration. For each view, the gain, compression and focus should be optimized so that the best echocardiographic image of the endocardial borders is obtained.
- Use echo contrast if available for images with suboptimal endocardial definition
- The sweep speed for all spectral Doppler and M-mode recordings should be 100 mm/sec. NOTE: at least 3 consecutive sinus beats and at least 5 consecutive "irregular rhythm" beats must be captured, so adjust the number of captures accordingly.
- As defined in the ASE Guidelines for the Quantification of Native Valve Regurgitation, Nyquist settings for color Doppler assessment of the cardiac valves should be 50-60 cm/sec.
- We encourage you to perform measurements as needed for clinical feedback to treating physicians. If you do perform on-line measurements, please do not obscure the flow profiles of subsequent beats. We suggest storing BOTH measured and unmeasured Doppler spectra and images.

- Once the data storage/file save operation is complete, transmit the data to the Core Lab, utilizing the instruction documentation provided in the AG Mednet Desktop Agent.
    - De-identify the images through the AG Mednet while uploading data. Enter the subject information as specified on the Echo Tracking Form. Importantly, the height and weight will have to be entered at every follow-up interval. Please measure and note the blood pressure on the subject ID screen or as an annotation on one or more images.

EXAMINATION SEQUENCE:

I. **Parasternal Long Axis of LV, LVOT, and MV**

- 2D (Image A below)
- Color Doppler of Aortic valve
- Color Doppler of Mitral Valve for mitral regurgitation
- Magnified views of LVOT and aortic valve – to identify the true LVOT dimension
- Magnify Mitral valve
- Obtain an RV inflow view



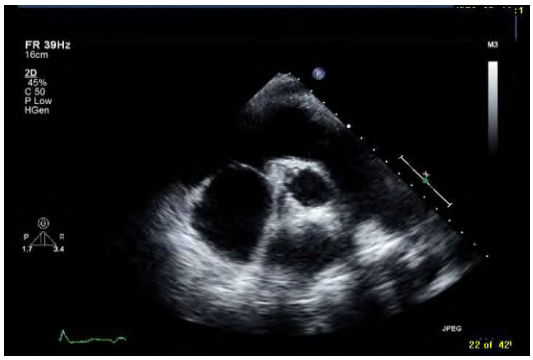
A. B.

II. **Parasternal Short axis at LV level**

- 2d should be obtained at 4 levels: apex, mid-papillary muscle, mitral valve, and LV outflow tract
- Color Doppler the Mitral valve for regurgitation at the mitral valve and LVOT level views.

III. Parasternal Short axis at aortic valve level

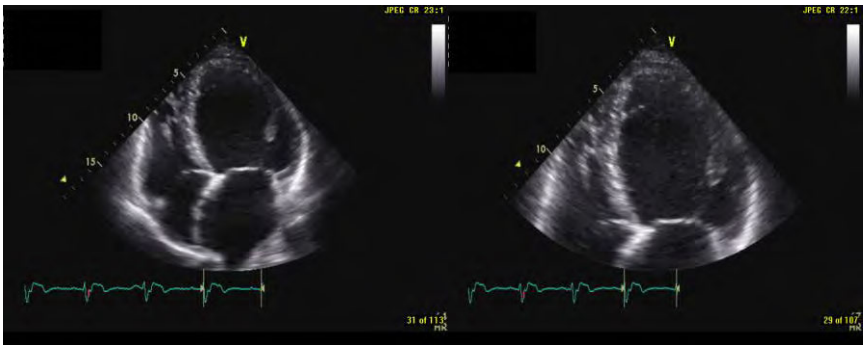
- 2D
- Zoom image of Aortic Valve
- Color Doppler of aortic valve
- Color Doppler of tricuspid valve



IV. Apical 4 chamber

- 2D optimizing LV endocardial borders: Need to see all aspects of the lateral wall, septum, and apex
- Zoom image of Mitral valve
- Show a loop with decreased depth such that LV occupies most of the imaging sector ensuring all walls are visualized
- Color Doppler of MR showing entire left atrium (to allow jet dimension/LA measurement)

- Provide components for PISA calculation
  - CW of MR jet
  - PW of MR jet
  - Zoomed PISA display (baseline shift down to optimize hemispherical PISA shell)
  - The aliasing velocity of color scale should be shifted down or towards MR jet to around 40cm/sec
  - If possible, provide split screen (color suppress) images (i.e. one side with color, one without)
  - Pulse wave Doppler the mitral valve inflow. Maximize spectral Doppler wave form to provide a large enough tracing to make calculations.
  - Continuous wave Doppler the mitral valve inflow. Maximize spectral Doppler wave form to provide a large enough tracing to make calculations.
- Color flow Doppler of tricuspid valve
- Continuous wave Doppler of TV

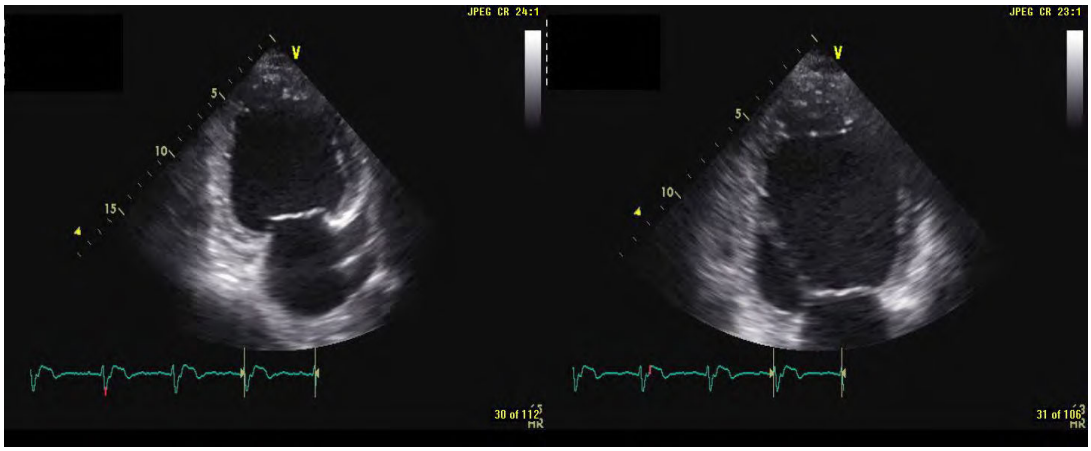


V. Apical 5 chamber view

- 2D image of apical 5 chamber
- Pulse wave Doppler of LVOT **(to avoid the region of flow acceleration - sample volume should be positioned at valve level and then moved apically until valve noise or "clicks" are no longer detected and then recorded for the baseline study)**
- Continuous wave Doppler through the aortic valve
- Note: record a full screen 2D image showing the pulse wave sample position (either as moving image or still frame) as well as the Pulse Wave Spectral Doppler for each position. It is very difficult to establish the sample volume position from the small image that is available when image and spectral display are provided simultaneously.

VI. Apical 2 chamber

- 2D optimizing LV endocardial borders: Need to see all aspects of the anterior wall, inferior wall, and apex
- Zoom image of Mitral valve
- Show a loop with decreased depth such that LV occupies most of the imaging sector ensuring all walls are visualized
- Color Doppler of MR

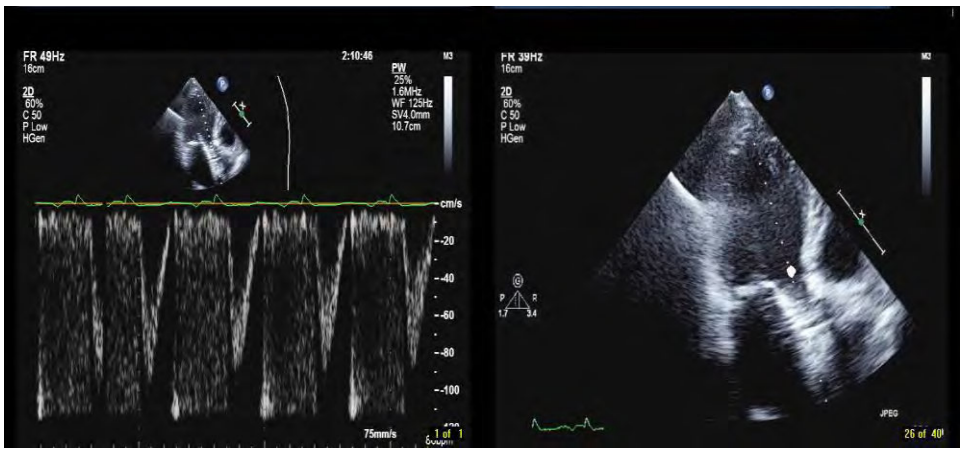


A. B.

** Image A shows the traditional 2 chamber while image B shows the 2 chamber with decreased depth*

VII. Apical long axis view (also known as 3 chamber view)

- 2D image of apical long axis
- Color Doppler of Mitral valve
- Zoom image of mitral valve
- Pulse Wave Doppler just **apical to the valve frame** as specified in apical 5 chamber view
- Note: record a full screen 2D image showing the pulsed wave sample position (either as moving image or still frame) as well as the Pulse Wave Spectral Doppler for each position
- Continuous Wave Doppler through the aortic valve



A. B.

VIII. Non imaging transducer in apical window

- Continuous wave Doppler interrogation of the mitral valvular flow should also be obtained using the pedoff transducer

IX. Specific Comments on Imaging Planes

A. Parasternal long axis view is recorded with the transducer in the third or fourth intercostal space immediately to the left of the sternum. The transducer should be angled so that the aortic valve, mitral valve and left ventricle are in their long axis.

IMAGING TIP 1: PARASTERNAL LONG AXIS VIEW

It is important that the parasternal long axis view displays the true long axis of the ventricle with the left ventricle lying horizontally on the image. If it is impossible to obtain a single view which optimally displays the long axis of the aortic valve, mitral valve, and aortic root as well as the long axis of the left ventricle, record 2 separate views. It is unacceptable to record an off-axis view in which the apex "points up" on the screen. If this type of image is obtained try moving the transducer up 1-2 intercostal spaces or having the subject take a breath in. Sometimes having the subject move to a more lateral decubitus position will help as well.

IMAGING TIP 2: PARASTERNAL LONG AXIS VIEW

Measurement of the left ventricular outflow tract and aortic valve and mitral valve are the key components of the study.

B. Parasternal short axis view is obtained by angling the probe 90° with respect to the parasternal long axis of the LV. The goal of this view is to obtain information about the aortic valve, the mitral valve as well as the LV.

IMAGING TIP 3: PARASTERNAL SHORT AXIS VIEW

This is an essential view post-op to completely assess mitral regurgitation. This may be the only view in which prosthetic valve regurgitant jets are imaged. Imaging at the level of as well as just below the leaflets may allow you to better image these jets.

C. **Apical four-chamber** view provides considerable information including the relative sizes of the right and left ventricles and the regional function of the LV. The four chamber view is defined as a view which maximizes the LV long axis and the tricuspid and mitral annular dimensions. In this view, the full excursion of the mitral and tricuspid valves should be seen. The complete endocardial border of the LV will be traced for chamber volume assessment (method of discs) so all aspects including the apex should be visualized. In the apical four chamber view, color Doppler of mitral and tricuspid regurgitation should be recorded. The four chamber view should visualize the lateral, septal and apical walls.

D. **Apical two-chamber** view should be obtained for the goal of assessment of LV size and function. The complete endocardial border of the LV will be traced for chamber volume assessment (method of discs) so all aspects including the apex should be visualized. The degree of MR by color Doppler will also be assessed. The two chamber view should visualize the anterior, inferior and apical walls.

IMAGING TIP 4: APICAL 4 and 2 CHAMBER VIEWS

Because we will measure volumes from the apical views as an important end-point of the study, please try to avoid apical foreshortening. If the view appears to be foreshortened, please bring the transducer down one intercostal space and have the subject take a breath in (particularly for the apical two-chamber view). Sometimes this will bring out a better (not foreshortened) view.

E. **Apical 5 chamber and 3 chamber** views are obtained to provide detailed information about the aortic valve and mitral valve color, and the spectral and continuous wave Doppler.

IMAGING TIP 5: APICAL 5 and 3 CHAMBER VIEWS

Both these views are essential in imaging post-device mitral regurgitant jets. Because we will be measuring jet vena contracta and jet length, a Res/Zoom view which includes imaging of the entire jet would be helpful. In addition, the 3Ch view may be used in the biplane Simpson's calculation of LV volume when the 2Ch view is inadequate. Thus, careful attention to endocardial definition is important.

XI. Abbreviations

2D=Two-dimensional
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MV=Mitral Valve
PI=Performance Index
PW=Pulse wave
SV=Stroke Volume
TR=Tricuspid Regurgitation
TVI or VTI=Time Velocity Integral

4. Site Echocardiographer Checklist

Labeling and Demographics:

Subject Study ID: _____

Visit: Baseline Operative Discharge POD 105
POD 390 2 yr 3yr 4yr 5yr
6 yr 7 yr 8 yr 9 yr 10 yr
Interim (Specify Reason): _____

Exam Date __ __/__ __ __/__ __ (Day/Month/Year)
Height: _____ cm
Weight: _____ kg
Heart Rate: _____ bpm
Rhythm: _____
Blood Pressure (mmHg):
Systolic_____
Diastolic_____

I. Parasternal Long Axis of LV, LVOT, MV views
- ☐ 2D
- ☐ Color Doppler of Mitral Valve for MR
- ☐ Magnified views of LVOT and aortic valve
- ☐ Magnified view of Mitral valve

II. Parasternal Short axis at LV level
- ☐ LV apex,
- ☐ LV mid-papillary muscle
- ☐ LV Mitral valve
- ☐ LVOT
- ☐ Color Doppler of the Mitral valve for regurgitation at the mitral valve and LVOT level

III. Parasternal Short axis at AV level
- ☐ 2D
- ☐ Color Doppler of TR (optional)

IV. Apical 4 chamber
- ☐ 2D optimizing LV endocardial borders
- ☐ LV with decreased depth
- ☐ Zoom Mitral valve
- ☐ Color Doppler of Mitral valve
- ☐ Color Doppler of TR (with CW)
- ☐ PISA information for mitral valve

V. Apical 5 chamber view

- ☐ Pulsed Wave Doppler of LVOT (multiple levels)
- ☐ Continuous wave Doppler through the AV

VI. Apical 2 chamber

- ☐ 2D optimizing LV endocardial borders
- ☐ LV with decreased depth
- ☐ Zoom Mitral valve
- ☐ Color Doppler of Mitral valve

VII. Apical long axis (3 chamber) view

- ☐ 2 D optimizing LV endocardial borders
- ☐ LV with decreased depth
- ☐ Zoom Mitral valve
- ☐ Pulsed Wave Doppler at the LVOT
- ☐ Continuous Wave Doppler through AV
- ☐ Color Doppler of Mitral valve for MR

VIII. Non imaging transducer in apical window

- ☐ Continuous wave Doppler interrogation of the Mitral valvular flow should also be obtained using the pedoff transducer

5.Core Lab Echo Tracking Form

An Echo Tracking Form will be completed for each subject including the following information, and will be submitted along with the echo data via AG Mednet (vendor providing digital transfer of echo data) to the Core Lab:

1. Follow-up interval
2. Exam transfer date
3. Exam date
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5. Site number
6. Echo type: TTE/ TEE
7. Heart rate (bpm)
8. Cardiac rhythm
9. Site comments
10. Name and email of person completing form
11. Scan date
12. Date completed
13. DICOM scan date
14. Echo scanner manufacturer name and model
15. Subject height (cm) and weight (kg)

6.Site Data Collection/ Entry into Oracle EDC (Echo Tracking Form)

Each echocardiogram should also be read by the sites and data should be entered on the appropriate case report form (CRF). Data to be reported in addition to what is requested in the Echo Tracking Form include the following measurements:

- Subject blood pressure (systolic and diastolic)

- LVOT assessment:
  - Peak velocity
  - Peak gradient
  - Mean gradient
  - VTI

- Mitral valve assessment:
  - Peak velocity
  - Peak gradient
  - Mean gradient
  - VTI
  - Annulus size (cm)
  - MV area (cm^2)

- Mitral regurgitation severity (Paravalvular, Transvalvular and Total Insufficiency/Regurgitation)

- 0 None
- +1 Trivial/Trace
- +2 Mild
- +3 Moderate
- +4 Severe
- Indeterminate

- Non-study valve regurgitation severity
  - 0 None
  - +1 Trivial/Trace
  - +2 Mild
  - +3 Moderate
  - +4 Severe
  - Indeterminate

- LVEF
  - Range of LVEF
  - Method used to determine LVEF (single plane or biplane)

- Assessment of RV function
  - Normal
  - Mildly reduced
  - Severely reduced
  - Indeterminate

- Method of delivery of echocardiographs to Core Lab
  - Images uploaded, FedEx, UPS, DHL, Other
  - Tracking number

7. Shipping & Contact Information

A copy of all documents and data must be kept at your site. Documents and CD's must be labeled with the trial protocol number (Protocol # 2012-02), the site ID, subject ID, subject initials, exam date, and exam interval.

Though all data is preferred to be uploaded digitally via AG Mednet, if shipping CDs, please send us an e-mail at when you ship your package. Upon its receipt, an official e-mail notification will be sent from the Core Lab to your site coordinator. Please confirm that the e-mail notification correlates with your shipping records. You should contact the Core Lab immediately with any discrepancies or if you have shipped a study but you have not received an e-mail notification within 2 business days.

Please do not hesitate to contact us with any questions. For non-urgent communications, e-mail is typically the best means.

For echo-related urgent questions, please call

We are looking forward to being your partners in this important clinical trial.

ATTACHMENT F – SERUM GLYCEROL SAMPLE COLLECTION MANUAL

No Longer In Use

ATTACHMENT G – QUALITY OF LIFE QUESTIONNAIRE

(SF-12 V2)

No Longer In Use

ATTACHMENT H – ADVERSE EFFECT (CODES & DEFINITIONS)

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.1	**BLOOD AND LYMPHATIC (INCLUDING ALL BLEEDING COMPLICATIONS)**	
AE101	ANEMIA – NON-BLEEDING RELATED	A CONDITION IN WHICH RED BLOOD CELL COUNT AND/OR HEMOGLOBIN ARE LESS THAN NORMAL DUE TO LACK OF PRODUCTION OF RED BLOOD CELLS, AND THAT REQUIRES TREATMENT OR TRANSFUSION.
AE102	ANEMIA – BLEEDING RELATED - MAJOR	A CONDITION IN WHICH RED BLOOD CELL COUNT AND/OR HEMOGLOBIN ARE LESS THAN NORMAL DUE TO BLOOD LOSS, AND THAT REQUIRES TREATMENT OR TRANSFUSION.
AE103	ANEMIA – BLEEDING RELATED - MINOR	A CONDITION IN WHICH RED BLOOD CELL COUNT AND/OR HEMOGLOBIN ARE LESS THAN NORMAL DUE TO BLOOD LOSS, AND THAT REQUIRES TREATMENT OR TRANSFUSION.
AE104	BLEEDING - CARDIOVASCULAR - MAJOR	ANY EPISODE OF MAJOR INTERNAL OR EXTERNAL BLEEDING THAT CAUSES DEATH, HOSPITALIZATION, OR PERMANENT INJURY (E.G., VISION LOSS) OR NECESSITATES TRANSFUSION, PERICARDIOCENTESIS, OR REOPERATION. MAJOR BLEEDING UNEXPECTEDLY ASSOCIATED WITH MINOR TRAUMA SHOULD BE REPORTED AS A BLEEDING EVENT, BUT BLEEDING ASSOCIATED WITH MAJOR TRAUMA OR A MAJOR OPERATION (INCLUDING THE INDEX PROCEDURE) SHOULD NOT. THE LOCATION OF THE BLEEDING (GASTROINTESTINAL, GENITOURINARY, ETC.) MUST BE REPORTED. FOR EACH REPORTED BLEEDING EVENT, INDICATE IF SUBJECT IS TAKING ANTICOAGULANTS OR ANTI-PLATELET AGENTS.
AE105	BLEEDING - CARDIOVASCULAR - MINOR	"
AE106	BLEEDING - GENITOURINARY - MAJOR	"
AE107	BLEEDING - GENITOURINARY - MINOR	"
AE108	BLEEDING - GASTROINTESTINAL UPPER -MAJOR	"
AE109	BLEEDING - GASTROINTESTINAL UPPER -MINOR	"
AE110	BLEEDING - GASTROINTESTINAL LOWER -MAJOR	"
AE111	BLEEDING - GASTROINTESTINAL LOWER -MINOR	"
AE112	BLEEDING - MUSCULOSKELETAL/DERMATOLOGICAL -MAJOR	" (E.G. ECCHYMOSIS)
AE113	BLEEDING - MUSCULOSKELETAL/DERMATOLOGICAL -MINOR	" (E.G. ECCHYMOSIS)
AE114	BLEEDING - NEUROLOGICAL - MAJOR	" (E.G. CEREBRAL VASCULAR ACCIDENT)
AE115	BLEEDING - NEUROLOGICAL - MINOR	" (E.G. CEREBRAL VASCULAR ACCIDENT)
AE116	BLEEDING - PERIPHERAL VASCULAR -MAJOR	" (E.G. NOSEBLEEDS; HEMATOMAS)
AE117	BLEEDING - PERIPHERAL VASCULAR - MINOR	" (E.G. NOSEBLEEDS; HEMATOMAS)
AE118	BLEEDING - PULMONARY/RESPIRATORY - MAJOR	" (E.G. HEMOTHORAX)
AE119	BLEEDING - PULMONARY/RESPIRATORY MINOR	" (E.G. HEMOTHORAX)
AE120	BLOOD SEPSIS	POSITIVE BLOOD CULTURE AND CLINICAL EVIDENCE OF INFECTION (E.G. FEVER, ELEVATED WBC COUNT, HYPOTENSION, END ORGAN DYSFUNCTION) EVENT MUST BE CONFIRMED BY 2 CONSECUTIVE POSITIVE BLOOD CULTURES, EXPLANT OR AUTOPSY.

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.1	**BLOOD AND LYMPHATIC (INCLUDING ALL BLEEDING COMPLICATIONS)** ***(CONTINUED)***	
AE122	HEMOLYSIS WITHOUT PARAVALVULAR LEAK	PLASMA -FREE HEMOGLOBIN > 40 MG/DL ON TWO CONSECUTIVE MEASUREMENTS WITHIN 48 HOURS; OR CLINICAL DIAGNOSIS OF HEMOLYSIS EVIDENCED BY LABORATORY TESTING SUCH AS SERUM HEMOGLOBIN, HEMATOCRIT, AND/OR PLASMA-FREE HEMOGLOBIN (NOT IMMUNOLOGICALLY BASED)
AE123	DISSEMINATED INTRAVASCULAR COAGULATION (DIC)	DIFFUSE, NONSURGICAL, MICROVASCULAR HEMORRHAGE AND/OR THROMBOSES.
AE124	THROMBOCYTOPENIA – HEPARIN INDUCED (HIT)	THROMBOCYTOPENIA (<150,000 PER CUBIC MILLIMETER), OR A RELATIVE DECREASE OF 50 PERCENT OR MORE FROM BASELINE, OR NEW THROMBOSIS IN A SUBJECT RECEIVING HEPARIN OR LMWH; CONFIRMED BY SEROLOGIC TESTING FOR PF4–HEPARIN ANTIBODIES.
AE125	THROMBOCYTOPENIA – NON-HEPARIN INDUCED	THROMBOCYTOPENIA (<150,000 PER CUBIC MILLIMETER), OR A RELATIVE DECREASE OF 50 PERCENT OR MORE FROM BASELINE, ACCOMPANIED BY A LOW INDEX OF SUSPICION FOR HIT (I.E., NOT ASSOCIATED WITH HEPARIN USE, THE PRESENCE OF OTHER CAUSES OF THROMBOCYTOPENIA, SUCH AS DRUGS OTHER THAN HEPARIN, DIC OR OTHER CONSUMPTIVE PROCESSES, POST-TRANSFUSION PURPURA).
AE126	BLOOD/ LYMPHATIC - OTHER	OTHER BLOOD OR LYMPHATIC EVENT THAT DOES NOT FIT IN ONE OF THE OTHER "BLOOD" CATEGORIES THAT REQUIRES HOSPITALIZATION OR MEDICAL INTERVENTION.
AE.2	**CARDIOVASCULAR - ARRHYTHMIA**	
AE158	ARRHYTHMIA - PERMANENT ATRIAL FIBRILLATION	AN ABNORMAL HEARTBEAT IN WHICH THE HEART RHYTHM IS FAST AND IRREGULARLY IRREGULAR. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS. AF IS CONSIDERED PERMANENT WHEN IT HAS PERSISTED BEYOND 1 YEAR AND ATTEMPTS AT CARDIOVERSION HAVE FAILED OR COULD NOT BE ATTEMPTED.
AE149	ARRHYTHMIA - PAROXYSMAL ATRIAL FIBRILLATION (PAF)	AN ABNORMAL HEARTBEAT IN WHICH THE HEART RHYTHM IS FAST AND IRREGULARLY IRREGULAR. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS. AF IS CONSIDERED PAROXYSMAL WHEN EPISODES OF AF TERMINATE SPONTANEOUSLY WITHIN 7 DAYS (MOST EPISODES LAST LESS THAN 24 HOURS)
AE157	ARRHYTHMIA - PERSISTENT ATRIAL FIBRILLATION	AN ABNORMAL HEARTBEAT IN WHICH THE HEART RHYTHM IS FAST AND IRREGULARLY IRREGULAR. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS . AF IS CONSIDERED PERSISTENT WHEN EPISODES OF AF LAST MORE THAN 7 DAYS AND MAY REQUIRE EITHER PHARMACOLOGIC OR ELECTRICAL INTERVENTION TO TERMINATE
AE141	ARRHYTHMIA - ATRIAL FLUTTER	WELL ORGANIZED BUT OVERLY RAPID CONTRACTIONS OF HEART ATRIUM (USUALLY AT A RATE OF 250-350 CONTRACTIONS PER MINUTE). EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE142	ARRHYTHMIA - AV BLOCK - 1ST DEGREE	AV BLOCK I: A CONDUCTION DISORDER OF NERVOUS IMPULSE AT THE LEVEL OF THE ATRIOVENTRICULAR JUNCTION, I.E. BETWEEN ATRIUM AND VENTRICLE.
AE143	ARRHYTHMIA - AV BLOCK - 2ND DEGREE	" AV BLOCK II: THERE ARE TWO TYPES: MOBITZ I PROGRESSIVE PROLONGATION OF PR INTERVAL WITH DROPPED BEATS (THE PR INTERVAL GETS LONGER AND LONGER; FINALLY ONE BEAT DROPS) MOBITZ II PR INTERVAL REMAINS UNCHANGED PRIOR TO THE P-WAVE WHICH SUDDENLY FAILS TO CONDUCT TO THE VENTRICLES;
AE144	ARRHYTHMIA - AV BLOCK - 3RD DEGREE	" AV BLOCK III: , NO P-WAVES CONDUCT TO THE VENTRICLE AND AV DISSOCIATION IS COMPLETE. ANY LEVEL OF AV BLOCK EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE145	ARRHYTHMIA - BUNDLE BRANCH BLOCK - LEFT	BUNDLE BRANCH BLOCK IS AN INTRAVENTRICULAR CONDUCTION DEFECT (IVCD) THAT DISRUPTS THE NORMAL FLOW OF ELECTRICAL IMPULSES THAT RESULT IN A NORMAL HEART BEAT. QRS DURATION OF GREATER THAN 110 MILLISECONDS IS A DIAGNOSTIC INDICATION OF BBB. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.2	**CARDIOVASCULAR – ARRHYTHMIA *(CONTINUED)***	
AE146	ARRHYTHMIA - BUNDLE BRANCH BLOCK - RIGHT	"
AE147	ARRHYTHMIA - SUPRAVENTRICULAR TACHYCARDIA (SVT)	SUSTAINED TACHYARRHYTHMIA IN WHICH THE QRS APPEARS NORMAL AND HAS DURATION OF < 120 MSEC. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE148	ARRHYTHMIA - PAROXYSMAL ATRIAL TACHYCARDIA (PAT)	A RAPID HEART RHYTHM ORIGINATING ABOVE THE VENTRICULAR TISSUE DUE TO AV NODAL REENTRANT TACHYCARDIA. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE150	ARRHYTHMIA - VENTRICULAR FIBRILLATION	A RAPID IRREGULAR VENTRICULAR RHYTHM DUE TO MULTIPLE REENTRANT ACTIVITIES ASSOCIATED WITH ESSENTIALLY ZERO CARDIAC OUTPUT. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE151	ARRHYTHMIA - TACHYCARDIA - VENTRICULAR	AN ABNORMALLY FAST HEART RATE (TYPICALLY DEFINED AS >100 BPM IN ADULTS) WHICH MAY REQUIRE IMPLANT OF A PACEMAKER TO MAINTAIN A NORMAL HEART RATE. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS. VENTRICULAR TACHYCARDIA: DEFINED AS A REGULAR HEART RHYTHM ORIGINATING FROM THE VENTRICLE WITH A FREQUENCY OF 160 TO 200 BEATS PER MINUTE. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE152	ARRHYTHMIA - TACHYCARDIA - NON-VENTRICULAR	ASSUMED "
AE153	ARRHYTHMIA - BRADYCARDIA	AN ABNORMALLY SLOW HEART RATE (TYPICALLY DEFINED AS <60 BPM IN ADULTS) EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE154	ARRHYTHMIA - TACHY-BRADYCARDIA	A VARIANT OF SICK SINUS SYNDROME IN WHICH SLOW ARRHYTHMIAS AND FAST ARRHYTHMIAS ALTERNATE. EVENT SHOULD BE DOCUMENTED AND CONFIRMED BY ECG TEST RESULTS.
AE155	ARRHYTHMIA - PACEMAKER/ICD MALFUNCTION	PACEMAKER/ICD DOES NOT FUNCTION AS INTENDED.
AE156	ARRHYTHMIA - OTHER	ARRHYTHMIA THAT IS NOT COVERED BY ANY OF THE DEFINITIONS ABOVE. PLEASE SPECIFY
AE.3	**CARDIOVASCULAR - REGURGITATION**	
	IF THE VALVE INVOLVED IS THE STUDY VALVE, THEN THIS DEFINITION SHOULD BE USED, BUT THE EVENT SHOULD BE REPORTED AS STRUCTURAL OR NON-STRUCTURAL VALVE DYSFUNCTION (AS APPROPRIATE) REGURGITATION, AORTIC: ALSO KNOWN AS AORTIC INSUFFICIENCY AND INCOMPETENCE OF THE AORTIC VALVE, IN WHICH A PORTION OF THE LEFT VENTRICULAR FORWARD STROKE VOLUME RETURNS TO THE CHAMBER DURING DIASTOLE. THIS CATEGORY DOES NOT INCLUDE PARAVALVULAR LEAK, WHICH SHOULD BE CAPTURED UNDER NON-STRUCTURAL VALVE DYSFUNCTION. REGURGITATION, CENTRAL: OCCURS WHEN THE VALVE LEAFLETS DO NOT COMPLETELY CLOSE AND ALLOW SOME BLOOD TO LEAK BACK INTO THE HEART. REGURGITATION, INDETERMINATE: OCCURS WHEN BLOOD LEAKS BACK INTO THE HEART AND CANNOT BE CATEGORIZED BY LOCATION AND OR SEVERITY. REGURGITATION, MITRAL: ALSO KNOWN AS MITRAL INCOMPETENCE AND MITRAL INSUFFICIENCY IN WHICH THE BLOOD FLOWS BACKWARDS THROUGH THE MITRAL VALVE EACH TIME THE LEFT VENTRICLE CONTRACTS. DIAGNOSED BY AUSCULTATION (MURMUR) OR ECHOCARDIOGRAPHY. REGURGITATION, TRICUSPID: INSUFFICIENCY OF THE TRICUSPID VALVE CAUSING BLOOD FLOW FROM THE RIGHT VENTRICLE TO THE RIGHT ATRIUM DURING SYSTOLE.	
AE160	REGURGITATION - AORTIC-CENTRAL/TRANSVALVULAR-+1	TRIVIAL/TRACE
AE161	REGURGITATION - AORTIC-CENTRAL/TRANSVALVULAR-+2	MILD
AE162	REGURGITATION - AORTIC-CENTRAL/TRANSVALVULAR-+3	MODERATE
AE163	REGURGITATION - AORTIC-CENTRAL/TRANSVALVULAR-+4	SEVERE
AE168	REGURGITATION - AORTIC-INDETERMINATE-+1	TRIVIAL/TRACE

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.3	**CARDIOVASCULAR - REGURGITATION *(CONTINUED)***	
AE169	REGURGITATION - AORTIC-INDETERMINATE-+2	MILD
AE170	REGURGITATION - AORTIC-INDETERMINATE-+3	MODERATE
AE171	REGURGITATION - AORTIC-INDETERMINATE-+4	SEVERE
AE172	REGURGITATION - MITRAL-CENTRAL/TRANSVALVULAR-+1	TRIVIAL/TRACE
AE173	REGURGITATION - MITRAL-CENTRAL/TRANSVALVULAR-+2	MILD
AE174	REGURGITATION - MITRAL-CENTRAL/TRANSVALVULAR-+3	MODERATE
AE175	REGURGITATION - MITRAL-CENTRAL/TRANSVALVULAR-+4	SEVERE
AE180	REGURGITATION - MITRAL-INDETERMINATE-+1	TRIVIAL/TRACE
AE181	REGURGITATION - MITRAL-INDETERMINATE-+2	MILD
AE182	REGURGITATION - MITRAL-INDETERMINATE-+3	MODERATE
AE183	REGURGITATION - MITRAL-INDETERMINATE-+4	SEVERE
AE190	REGURGITATION - PULMONARY-CENTRAL/TRANSVALVULAR-+1	TRIVIAL/TRACE
AE191	REGURGITATION - PULMONARY-CENTRAL/TRANSVALVULAR-+2	MILD
AE192	REGURGITATION - PULMONARY-CENTRAL/TRANSVALVULAR-+3	MODERATE
AE193	REGURGITATION - PULMONARY-CENTRAL/TRANSVALVULAR-+4	SEVERE
AE198	REGURGITATION - PULMONARY-INDETERMINATE-+1	TRIVIAL/TRACE
AE199	REGURGITATION - PULMONARY-INDETERMINATE-+2	MILD
AE200	REGURGITATION - PULMONARY-INDETERMINATE-+3	MODERATE
AE201	REGURGITATION - PULMONARY-INDETERMINATE-+4	SEVERE
AE202	REGURGITATION - TRICUSPID-CENTRAL/TRANSVALVULAR-+1	TRIVIAL/TRACE
AE203	REGURGITATION - TRICUSPID-CENTRAL/TRANSVALVULAR-+2	MILD
AE204	REGURGITATION - TRICUSPID-CENTRAL/TRANSVALVULAR-+3	MODERATE
AE205	REGURGITATION - TRICUSPID-CENTRAL/TRANSVALVULAR-+4	SEVERE
AE210	REGURGITATION - TRICUSPID-INDETERMINATE-+1	TRIVIAL/TRACE
AE211	REGURGITATION - TRICUSPID-INDETERMINATE-+2	MILD
AE212	REGURGITATION - TRICUSPID-INDETERMINATE-+3	MODERATE
AE213	REGURGITATION - TRICUSPID-INDETERMINATE-+4	SEVERE

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.5	**CARDIOVASCULAR - STENOSIS**	***IF THE VALVE INVOLVED IS THE STUDY VALVE, THEN THIS DEFINITION SHOULD BE USED, BUT THE EVENT SHOULD BE REPORTED AS STRUCTURAL OR NON-STRUCTURAL VALVE DYSFUNCTION (AS APPROPRIATE)**
AE220*	STENOSIS - AORTIC - MILD	AORTIC: FLOW OBSTRUCTION OF THE AORTIC VALVE DUE TO RESTRICTED LEAFLET OPENING. THE SEVERITY IS CATEGORIZED AS: MILD - JET VELOCITY (M/S) <3.0; MEAN GRADIENT (MMHG) <25; VALVE AREA (CM2) >1.5.MODERATE - JET VELOCITY (M/S) 3.0-4.0; MEAN GRADIENT (MMHG) 25-40; VALVE AREA (CM2) 1.0- 1.5. OR SEVERE - JET VELOCITY (M/S) >4.0; MEAN GRADIENT (MMHG) >40; VALVE AREA (CM2) <1.0; VALVE AREA INDEX<0.6. MITRAL: MITRAL STENOSIS (MS) REFERS TO NARROWING OF THE MITRAL VALVE ORIFICE, RESULTING IN IMPEDANCE OF FILLING OF THE LEFT VENTRICLE IN DIASTOLE. THE SEVERITY OF MS IS CATEGORIZED AS: MILD - MEAN GRADIENT (MM HG) < 5, PULMONARY ARTERY SYSTOLIC PRESSURE (MM HG) < 30, VALVE AREA (CM2) >1.5. MODERATE - MEAN GRADIENT (MM HG) 5-10, PULMONARY ARTERY SYSTOLIC PRESSURE (MM HG) 30-50, VALVE AREA (CM2) 1.0-1.5. SEVERE - MEAN GRADIENT (MM HG) > 10, PULMONARY ARTERY SYSTOLIC PRESSURE (MM HG)> 50, VALVE AREA (CM2) <1.0. TRICUSPID: A NARROWING OF THE TRICUSPID VALVE OPENING THAT INCREASES RESISTANCE TO BLOOD FLOW FROM THE RIGHT ATRIUM TO THE RIGHT VENTRICLE. SEVERE TRICUSPID STENOSIS IS DEFINED AS A VALVE AREA LESS THAN 1.0 CM2.
AE221*	STENOSIS - AORTIC - MODERATE	"
AE222*	STENOSIS - AORTIC - SEVERE	"
AE223	STENOSIS - MITRAL- MILD	"
AE224	STENOSIS - MITRAL - MODERATE	"
AE225	STENOSIS - MITRAL - SEVERE	"
AE226	STENOSIS - PULMONARY- MILD	"
AE227	STENOSIS - PULMONARY - MODERATE	"
AE228	STENOSIS - PULMONARY - SEVERE	"
AE229	STENOSIS - TRICUSPID- MILD	"
AE230	STENOSIS - TRICUSPID- MODERATE	"
AE231	STENOSIS - TRICUSPID - SEVERE	"

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.6	**CARDIOVASCULAR - THROMBOEMBOLIC EVENT/VALVE THROMBOSIS**	**ANY EMBOLIC EVENT THAT OCCURS IN THE ABSENCE OF INFECTION AFTER THE IMMEDIATE PERIOPERATIVE PERIOD AND MAY BE MANIFESTED BY A NEUROLOGIC EVENT OR A NON-CEREBRAL EMBOLIC EVENT. EMBOLI CONSISTING OF NON-THROMBOTIC MATERIAL (E.G., ATHEROSCLEROSIS, MYXOMA) ARE NOT COUNTED.**
AE250	THROMBOEMBOLIC EVENT – STROKE	INCLUDES ANY CENTRAL, NEW NEUROLOGIC DEFICIT, WHETHER TEMPORARY OR PERMANENT AND WHETHER FOCAL OR GLOBAL, THAT OCCURS AFTER THE SUBJECT EMERGES FROM ANESTHESIA. POSTOPERATIVE NEUROLOGIC SYMPTOMS THAT MIMIC THOSE OF A PREOPERATIVELY DOCUMENTED NEUROLOGIC EVENT AND THAT ARE CONFIRMED RADIOGRAPHICALLY TO BE CONSISTENT WITH THE FORMER EVENT ARE NOT COUNTED. CENTRAL NEUROLOGIC EVENTS THAT ARE CLEARLY RELATED TO AORTIC, INTERNAL CAROTID ARTERY, OR VERTEBRAL ARTERY DISEASE ARE ALSO NOT COUNTED. PSYCHOMOTOR DEFICITS FOUND BY SPECIALIZED TESTING ARE NOT CONSIDERED NEUROLOGIC EVENTS RELATED TO OPERATED VALVES. SUBJECTS WHO DO NOT AWAKEN OR WHO AWAKEN AFTER OPERATION WITH A NEW STROKE ARE NOT CONSIDERED TO HAVE SUSTAINED VALVE-RELATED NEUROLOGIC EVENTS. STROKE: A PROLONGED (>72 HOURS) OR PERMANENT NEUROLOGIC DEFICIT THAT IS USUALLY ASSOCIATED WITH ABNORMAL RESULTS OF MRI OR CT SCANS. SUBJECTS WITH MINIMAL, ATYPICAL, OR PROTEAN SYMPTOMS THAT LEAD TO RADIOGRAPHIC IMAGING DEMONSTRATING AN ACUTE ISCHEMIC EVENT ARE CONSIDERED TO HAVE SUSTAINED A STROKE. TIA: CHARACTERIZED BY FULLY REVERSIBLE SYMPTOMS OF SHORT DURATION. IF RADIOGRAPHIC IMAGING DEMONSTRATES AN ACUTE CENTRAL NEUROLOGIC LESION, HOWEVER, SUCH SUBJECTS ARE RECLASSIFIED AS HAVING SUSTAINED A STROKE.
AE255	THROMBOEMBOLIC EVENT – TRANSIENT ISCHEMIC ATTACK (TIA)	INCLUDES ANY CENTRAL, NEW NEUROLOGIC DEFICIT, WHETHER TEMPORARY OR PERMANENT AND WHETHER FOCAL OR GLOBAL, THAT OCCURS AFTER THE SUBJECT EMERGES FROM ANESTHESIA. POSTOPERATIVE NEUROLOGIC SYMPTOMS THAT MIMIC THOSE OF A PREOPERATIVELY DOCUMENTED NEUROLOGIC EVENT AND THAT ARE CONFIRMED RADIOGRAPHICALLY TO BE CONSISTENT WITH THE FORMER EVENT ARE NOT COUNTED. CENTRAL NEUROLOGIC EVENTS THAT ARE CLEARLY RELATED TO AORTIC, INTERNAL CAROTID ARTERY OR VERTEBRAL ARTERY DISEASE ARE ALSO NOT COUNTED. PSYCHOMOTOR DEFICITS FOUND BY SPECIALIZED TESTING ARE NOT CONSIDERED NEUROLOGIC EVENTS RELATED TO OPERATED VALVES. SUBJECTS WHO DO NOT AWAKEN OR WHO AWAKEN AFTER OPERATION WITH A NEW STROKE ARE NOT CONSIDERED TO HAVE SUSTAINED VALVE-RELATED NEUROLOGIC EVENTS. STROKE: A PROLONGED (>72 HOURS) OR PERMANENT NEUROLOGIC DEFICIT THAT IS USUALLY ASSOCIATED WITH ABNORMAL RESULTS OF MRI OR CT SCANS. SUBJECTS WITH MINIMAL, ATYPICAL, OR PROTEAN SYMPTOMS THAT LEAD TO RADIOGRAPHIC IMAGING DEMONSTRATING AN ACUTE ISCHEMIC EVENT ARE CONSIDERED TO HAVE SUSTAINED A STROKE. TIA: CHARACTERIZED BY FULLY REVERSIBLE SYMPTOMS OF SHORT DURATION. IF RADIOGRAPHIC IMAGING DEMONSTRATES AN ACUTE CENTRAL NEUROLOGIC LESION, HOWEVER, SUCH SUBJECTS ARE RECLASSIFIED AS HAVING SUSTAINED A STROKE.
AE256	THROMBOEMBOLIC EVENT - OTHER - PERIPHERAL NO PARESIS	A PERIPHERAL EMBOLIC EVENT IS AN OPERATIVE, AUTOPSY, OR CLINICALLY DOCUMENTED EMBOLUS THAT PRODUCES SYMPTOMS FROM COMPLETE OR PARTIAL OBSTRUCTION OF A PERIPHERAL (NON-CEREBRAL) ARTERY. LOCATION SHOULD BE REPORTED. REPORT UNDER PULMONARY EMBOLISM IF EVENT OCCURS IN THE LUNG.
AE257	THROMBOEMBOLIC EVENT - OTHER – PERIPHERAL	" HEMIPARESIS
AE258	THROMBOEMBOLIC EVENT - OTHER - PERIPHERAL	" FULL PARESIS
AE259	THROMBOEMBOLIC EVENT - OTHER - CENTRAL	" NO PARESIS
AE260	THROMBOEMBOLIC EVENT - OTHER – CENTRAL	" HEMIPARESIS
AE.6	**CARDIOVASCULAR - THROMBOEMBOLIC EVENT/VALVE THROMBOSIS *(CONTINUED)***	

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE261	THROMBOEMBOLIC EVENT - OTHER - CENTRAL	" FULL PARESIS
AE262	VALVE THROMBOSIS - AORTIC	ANY THROMBUS NOT CAUSED BY INFECTION ATTACHED TO OR NEAR AN OPERATED VALVE THAT OCCLUDES PART OF THE BLOOD FLOW PATH, INTERFERES WITH VALVE FUNCTION, OR IS SUFFICIENTLY LARGE TO WARRANT TREATMENT. VALVE THROMBUS FOUND AT AUTOPSY IN A SUBJECT WHOSE CAUSE OF DEATH WAS NOT VALVE RELATED OR FOUND AT OPERATION FOR AN UNRELATED INDICATION SHOULD ALSO BE COUNTED.
AE263	VALVE THROMBOSIS - MITRAL	"
AE264	VALVE THROMBOSIS - PULMONARY	"
AE265	VALVE THROMBOSIS - TRICUSPID	"
AE.7	**CARDIOVASCULAR - MISC**	
AE270	ANGINA, STABLE	CHEST PAIN, TIGHT OR HEAVY FEELING IN THE CHEST, OR DISCOMFORT WHICH SPREADS FROM THE CHEST TO THE ARM, BACK, NECK, JAW, OR STOMACH, NUMBNESS OR TINGLING IN THE SHOULDERS, ARMS OR WRISTS, SHORTNESS OF BREATH, AND NAUSEA RELIEVED BY REST OR NITROGLYCERINE AND/OR CONFIRMED BY ECG. STABLE ANGINA IS ANGINA THAT IS CONTROLLED BY ORAL AND/OR TRANSCUTANEOUS MEDICATION.
AE271	ANGINA, UNSTABLE	UNSTABLE ANGINA IS ANGINA, WHICH NECESSITATES THE INITIATION, CONTINUATION OR INCREASE OF ANGINA CONTROL THERAPIES THAT MAY INCLUDE: NITROGLYCERIN DRIP, HEPARIN DRIP, OR IABP PLACEMENT. THE TYPE OF ANGINA MAY INCLUDE, BUT IS NOT LIMITED TO: REST ANGINA, NEW ONSET EXERTIONAL ANGINA OF AT LEAST NEW YORK HEART ASSOCIATION (NYHA) CLASS III IN SEVERITY, RECENT ACCELERATION IN PATTERN AND INCREASE OF ONE NYHA CLASS TO AT LEAST NYHA CLASS III, VARIANT ANGINA, NON-Q WAVE MYOCARDIAL INFARCTION, OR POST-INFARCTION ANGINA.
AE272	ANNULAR DISSECTION	DISSECTION OF THE VALVULAR ANNULUS EXTENDING INTO THE AORTA. ANNULAR DISSECTION OCCURRING WITHIN 30 DAYS OF THE INDEX PROCEDURE WILL BE CONSIDERED VALVE RELATED. SHOULD BE CONFIRMED BY IMAGING, OR DIRECT VISUAL INSPECTION.
AE273	AORTIC DISSECTION	DISRUPTION OF THE MEDIA LAYER OF THE AORTA WITH BLEEDING WITHIN AND ALONG THE WALL OF THE AORTA. AORTIC DISSECTION MAY OCCUR IN THE ASCENDING THORACIC AORTA (TYPE A DISSECTION) OR IN THE DESCENDING THORACIC AORTA (TYPE B DISSECTION). DISSECTION SHOULD BE CONFIRMED BY IMAGING OR DIRECT VISUAL INSPECTION.
AE274	ARTERIAL DISSECTION	DISRUPTION OF THE MEDIA LAYER OF AN ARTERY OTHER THAN THE AORTA WITH BLEEDING WITHIN AND ALONG THE WALL OF THE VESSEL. SHOULD BE CONFIRMED BY IMAGING OR DIRECT VISUAL INSPECTION.
AE275	CARDIAC ARREST	CARDIAC ARREST DOCUMENTED BY ONE OF THE FOLLOWING: VENTRICULAR FIBRILLATION, RAPID VENTRICULAR TACHYCARDIA WITH HEMODYNAMIC INSTABILITY, ASYSTOLE.
AE276	CARDIAC DECOMPENSATION	AN INABILITY OF THE HEART TO MAINTAIN ADEQUATE CIRCULATION; IT IS MARKED BY DYSPNEA, VENOUS ENGORGEMENT, CYANOSIS AND EDEMA.
AE277	CARDIOGENIC SHOCK	A CLINICAL STATE OF HYPOPERFUSION SUSTAINED FOR GREATER THAN 30 MINUTES, WITH EITHER SYSTOLIC BLOOD PRESSURE < 80 MM HG, AND /OR CARDIAC INDEX < 1.8 DESPITE MAXIMAL TREATMENT (FLUIDS) OR REQUIRING INTRAVENOUS INOTROPES AND/OR PRESSOR AGENT OR AN INTRA-AORTIC BALLOON PUMP (IABP).
AE.7	**CARDIOVASCULAR - MISC *(CONTINUED)***	

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE278	CHORDAE TENDINEAE DAMAGE	
AE279	CORONARY ARTERY OSTIAL OBSTRUCTION	OBSTRUCTION OF THE CORONARY OSTIA. SHOULD BE CONFIRMED BY IMAGING AND THE SOURCE OF THE OBSTRUCTION (AORTIC VALVE, THROMBUS, ETC. SHOULD BE REPORTED.
AE280	ENDOCARDITIS	ANY INFECTION INVOLVING THE STUDY VALVE. THE DIAGNOSIS OF OPERATED VALVULAR ENDOCARDITIS IS BASED ON ONE OF THE FOLLOWING CRITERIA: (1) REOPERATION WITH EVIDENCE OF ABSCESS, PARAVALVULAR LEAK, PUS, OR VEGETATION CONFIRMED AS SECONDARY TO INFECTION BY HISTOLOGIC OR MICROBIOLOGIC STUDIES; (2) AUTOPSY FINDINGS OF ABSCESS, PUS, OR VEGETATION INVOLVING A REPAIRED OR REPLACED VALVE; OR (3) IN THE ABSENCE OF REOPERATION OR AUTOPSY, MEETING OF THE DUKE CRITERIA FOR ENDOCARDITIS [4]. MORBIDITIES ASSOCIATED WITH ACTIVE INFECTION, SUCH AS VALVE THROMBOSIS, THROMBOTIC EMBOLUS, BLEEDING EVENT, OR PARAVALVULAR LEAK, ARE INCLUDED UNDER THIS CATEGORY, BUT NOT COUNTED IN OTHER CATEGORIES OF MORBIDITY.
AE281	HEART FAILURE – ACUTE	ACUTE HEART FAILURE DESCRIBES EXACERBATED OR DECOMPENSATED HEART FAILURE, REFERRING TO EPISODES IN WHICH A SUBJECT IS CHARACTERIZED AS HAVING A CHANGE IN HEART FAILURE SIGNS AND SYMPTOMS RESULTING IN A NEED FOR URGENT THERAPY OR HOSPITALIZATION.
AE282	HEART FAILURE – CHRONIC (CHF)	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 DEMANDS OF THE BODY, ASSUMING THE EVIDENCE OF ADEQUATE VENOUS RETURN. EVENT IS CONFIRMED CLINICALLY OR BY DIAGNOSTIC TESTING.
AE283	HYPERTENSION – SYSTEMIC	DEFINED AS BLOOD PRESSURE > 140 /90 MM HG FOR SUBJECT WITHOUT DIABETES OR KIDNEY DISEASE; >130/80 MMHG FOR SUBJECTS ON 2 OCCASIONS WITH DIABETES OR RENAL DISEASE. UNLESS DUE TO PRESENCE OF MEDICATION , E.G. BETA BLOCKERS FOR 10 YEARS
AE284	HYPERTENSION – PULMONARY	MEAN PULMONARY ARTERY PRESSURE THAT IS GREATER THAN 25 MMHG AT REST AND/OR GREATER THAN 30 MMHG DURING EXERCISE CONFIRMED BY SWAN GANZ CATHETER OR DIAGNOSTIC PLACEMENT IN THE PULMONARY ARTERY BED AND CONDITION REQUIRES MEDICAL INTERVENTION TO RESOLVE OR TREAT THE CONDITION.
AE285	HYPOTENSION	ABNORMALLY LOW BLOOD PRESSURE. FOR AN ADULT, HYPOTENSION IS DEFINED AS BLOOD PRESSURE LESS THAN 90/50 MMHG.

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.7	**CARDIOVASCULAR - MISC *(CONTINUED)***	
AE286	MYOCARDIAL INFARCTION	AN ACUTE MYOCARDIAL INFARCTION IS EVIDENCED BY ANY OF THE FOLLOWING: 1. A RISE AND FALL OF CARDIAC BIOMARKERS (PREFERABLY TROPONIN) WITH AT LEAST ONE OF THE VALUES IN THE ABNORMAL RANGE (CK ≥ 5X ULN) TOGETHER WITH AT LEAST ONE OF THE FOLLOWING MANIFESTATIONS OF MYOCARDIAL ISCHEMIA: A) ISCHEMIC SYMPTOMS; B) ECG CHANGES INDICATIVE OF NEW ISCHEMIA (NEW ST-T CHANGES, NEW LEFT BUNDLE BRANCH BLOCK, OR LOSS OF R WAVE VOLTAGE); C) DEVELOPMENT OF PATHOLOGICAL Q WAVES IN 2 OR MORE CONTIGUOUS LEADS IN THE ECG (OR EQUIVALENT FINDINGS FOR TRUE POSTERIOR MI); D. IMAGING EVIDENCE OF NEW LOSS OF VIABLE MYOCARDIUM OR NEW REGIONAL WALL MOTION ABNORMALITY. 2. DEVELOPMENT OF NEW PATHOLOGICAL Q WAVES IN 2 OR MORE CONTIGUOUS LEADS IN THE ECG, WITH OR WITHOUT SYMPTOMS. 3. IMAGING EVIDENCE OF A REGION WITH NEW LOSS OF VIABLE MYOCARDIUM AT REST IN THE ABSENCE OF A NON-ISCHEMIC CAUSE. THIS CAN BE MANIFEST AS: A. ECHOCARDIOGRAPHIC, CT, MR, VENTRICULOGRAPHIC OR NUCLEAR IMAGING EVIDENCE OF LEFT VENTRICULAR THINNING OR SCARRING AND FAILURE TO CONTRACT APPROPRIATELY (I.E., HYPOKINESIS, AKINESIS, OR DYSKINESIS); OR, B. FIXED (NON-REVERSIBLE) PERFUSION DEFECTS ON NUCLEAR RADIOISOTOPE IMAGING (E.G., MIBI, THALLIUM).
AE287	MYOCARDITIS	AN INFECTION OF THE HEART MUSCLE
AE296	PERFORATION - ATRIAL	AN ABNORMAL HOLE OR OPENING IN THE ATRIAL WALL CAUSED BY A DEVICE CAUSING PUNCTURE THROUGH THE WALL OR BY PRESSURE AGAINST A WEAKENED PORTION OF THE WALL.
AE297	PERFORATION - VENTRICULAR	AN ABNORMAL HOLE OR OPENING IN THE VENTRICULAR WALL CAUSED BY A DEVICE CAUSING PUNCTURE THROUGH THE WALL OR BY PRESSURE AGAINST A WEAKENED PORTION OF THE WALL.
AE289	PERFORATION - OTHER	"
AE290	PERICARDIAL EFFUSION - MAJOR	EXCESS FLUID ACCUMULATION IN THE PERICARDIAL SPACE THAT INTERFERES WITH NORMAL HEART FUNCTION AND REQUIRES MEDICAL INTERVENTION TO RESOLVE. IT SHOULD BE CONFIRMED BY ECHOCARDIOGRAPHY OR CT.
AE291	PERICARDIAL EFFUSION - MINOR	"
AE292	PERICARDIAL TAMPONADE - MAJOR	ABNORMAL FLUID ACCUMULATION WITHIN THE PERICARDIAL SPACE THAT CAUSES HEMODYNAMIC COMPROMISE. THIS SHOULD BE DOCUMENTED BY EITHER: 1. ECHO SHOWING PERICARDIAL FLUID AND SIGNS OF TAMPONADE SUCH AS RIGHT HEART COMPROMISE. 2. SYSTEMIC HYPOTENSION DUE TO PERICARDIAL FLUID COMPROMISING CARDIAC FUNCTION.
AE294	PERICARDITIS	AN INFLAMMATION OF THE PERICARDIUM (THE FIBROUS SAC SURROUNDING THE HEART).
AE295	CARDIOVASCULAR - OTHER	

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.8	**GASTROINTESTINAL/HEPATIC**	
AE350	GASTROINTESTINAL – ESOPHAGEAL RUPTURE/TEAR	ANY EVIDENCE OF PUNCTURE/DISSECTION/PERFORATION, VARICES OR OTHER DAMAGE TO THE ESOPHAGUS REQUIRING INTERVENTION.
AE351	GASTROINTESTINAL – INFECTION	SEVERE INFLAMMATION OF THE GASTROINTESTINAL TRACT INVOLVING BOTH THE STOMACH AND SMALL INTESTINE RESULTING IN ACUTE DIARRHEA AND VOMITING. SHOULD BE CONFIRMED BY CULTURE
AE352	GASTROINTESTINAL – OTHER	OTHER GASTROINTESTINAL EVENT THAT DOES NOT FIT IN ONE OF THE OTHER GI/HEPATIC CATEGORIES.
AE353	LIVER FAILURE - ACUTE	A SYNDROME DEFINED BY THE OCCURRENCE OF ENCEPHALOPATHY, COAGULOPATHY AND JAUNDICE IN AN INDIVIDUAL WITH A PREVIOUSLY NORMAL LIVER.
AE354	LIVER FAILURE - CHRONIC	CHRONIC LIVER DISEASE CAUSES CAN BE ANY CONDITION THAT RESULTS IN THE GRADUAL DEGRADATION AND RENEWAL OF THE TISSUE CELLS WITH A BODY'S LIVER. THIS PROCESS USUALLY RESULTS IN FIBROSIS OR CIRRHOSIS. DIAGNOSIS MAY BE CONFIRMED BY ABNORMAL BLOOD ENZYMES AND/OR BIOPSY
AE355	HEPATIC COMPLICATION - OTHER	OTHER LIVER EVENTS THAT DO NOT MEET THE DEFINITION OF LIVER FAILURE (E.G. LIVER DYSFUNCTION) REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE356	PANCREATIC COMPLICATION (PANCREAS)	AN EVENT PERTAINING TO, CONNECTED WITH, OR AFFECTING THE PANCREAS REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE357	SPLENIC COMPLICATION (SPLEEN)	AN EVENT PERTAINING TO, CONNECTED WITH, OR AFFECTING THE SPLEEN REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE358	BILIARY (GALLBLADDER)	AN EVENT PERTAINING TO BILE OR TO THE GALLBLADDER AND BILE DUCTS, WHICH TRANSPORT BILE REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE359	ENDOCRINE COMPLICATIONS	AN EVENT PERTAINING TO, CONNECTED WITH, OR AFFECTING THE ENDOCRINE SYSTEM REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE360	METABOLIC COMPLICATIONS	AN EVENT PERTAINING TO, CONNECTED WITH, OR AFFECTING THE METABOLIC SYSTEM REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE.9	**GENITOURINARY/RENAL**	
AE370	URINARY TRACT INFECTION (UTI)	INFECTION THAT AFFECTS ANY PART OF THE URINARY TRACT THAT REQUIRE HOSPITALIZATION OR MEDICAL INTERVENTION.
AE371	VAGINAL INFECTION	INFECTIONS AFFECTING THE VAGINAL AREA THAT REQUIRE HOSPITALIZATION OR MEDICAL INTERVENTION.
AE372	GENITOURINARY – OTHER	OTHER GENITOURINARY EVENT NOT PREVIOUSLY DESCRIBED REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE373	RENAL DYSFUNCTION	AN ACUTE EVENT OR WORSENING OF RENAL FUNCTION POST-OPERATIVELY (INCREASE OF SERUM CREATININE TO < 2.0 , AND < 2X MOST RECENT PREOPERATIVE CREATININE LEVEL) AND DOES NOT REQUIRE DIALYSIS.

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.9	**GENITOURINARY/RENAL *(CONTINUED)***	
AE374	RENAL FAILURE – ACUTE	AN ACUTE EVENT OR WORSENING OF RENAL FUNCTION RESULTING IN ONE OR MORE OF THE FOLLOWING: 1) INCREASE OF SERUM CREATININE TO >2.0, AND 2X MOST RECENT PREOPERATIVE CREATININE LEVEL. 2) A NEW REQUIREMENT FOR DIALYSIS POSTOPERATIVELY.
AE375	RENAL FAILURE – CHRONIC	A PROGRESSIVE LOSS IN RENAL FUNCTION OVER A PERIOD OF MONTHS OR YEARS RESULTING IN A DIAGNOSIS OF STAGE 5 - CHRONIC KIDNEY DISEASE.
AE376	RENAL – OTHER	OTHER EVENT THAT IS NOT RENAL FAILURE OR RENAL DYSFUNCTION THAT REQUIRES HOSPITALIZATION OR MEDICAL INTERVENTION.
AE.10	**PULMONARY/RESPIRATORY**	
AE380	ATELECTASIS	COMPLETE OR PARTIAL COLLAPSE OF A PREVIOUSLY INFLATED LUNG; INABILITY OF LUNG TO FULLY EXPAND.
AE381	HYPOXEMIA	DECREASED PARTIAL PRESSURE OF OXYGEN IN BLOOD SOMETIMES SPECIFICALLY AS LESS THAN 60 MMHG (8.0 KPA) OR CAUSING HEMOGLOBIN OXYGEN SATURATION OF LESS THAN 90%.
AE382	PLEURAL EFFUSION - RIGHT	EXCESS ACCUMULATION OF FLUIDS, SOMETIMES BLOOD IN THE PLEURAL SPACE, WHICH IS COMMON AFTER CARDIAC SURGERY. REPORTABLE WHEN IT BECOMES SYMPTOMATIC AND REQUIRES FLUID TO BE INTERVENTIONALLY REMOVED.
AE383	PLEURAL EFFUSION - LEFT	"
AE384	PLEURAL EFFUSION - BILATERAL	"
AE385	PNEUMOTHORAX	ACCUMULATION OF AIR OR GAS IN THE PLEURAL CAVITY, OCCURRING BECAUSE OF DISEASE OR INJURY AND REQUIRING SURGICAL INTERVENTION, HOSPITALIZATION OR MEDICAL INTERVENTION TO RESOLVE.
AE386	PULMONARY EDEMA	AN ABNORMAL ACCUMULATION OF FLUID IN THE LUNGS REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION TO RESOLVE.
AE387	PULMONARY HYPERTENSION	MEAN PULMONARY ARTERY PRESSURE THAT IS GREATER THAN 25 MMHG AT REST AND/OR GREATER THAN 30 MMHG DURING EXERCISE CONFIRMED BY SWAN GANZ CATHETER OR DIAGNOSTIC PLACEMENT IN THE PULMONARY ARTERY BED AND CONDITION REQUIRES HOSPITALIZATION OR MEDICAL INTERVENTION TO RESOLVE.
AE388	PULMONARY REGURGITATION	THE BACKWARD FLOW OF BLOOD FROM THE PULMONARY ARTERY, THROUGH THE PULMONARY VALVE, AND INTO THE RIGHT VENTRICLE OF THE HEART DURING DIASTOLE.
AE389	PULMONARY EMBOLISM - RIGHT	CLINICAL EVIDENCE OF NEW EMBOLISM WITH CONFIRMATION BY LUNG SCAN OR PULMONARY ANGIOGRAPHY.
AE390	PULMONARY EMBOLISM - LEFT	"
AE391	PULMONARY EMBOLISM - BILATERAL	"
AE392	PULMONARY/RESPIRATORY - OTHER	OTHER RESPIRATORY EVENT THAT IS NOT RESPIRATORY FAILURE.
AE393	RESPIRATORY DYSFUNCTION/INSUFFICIENCY	DETERIORATION OF SUBJECT'S RESPIRATORY EFFORTS LESS THAN 24 HRS AFTER COMPLETION OF THE INDEX PROCEDURE.

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE.10	**PULMONARY/RESPIRATORY**	
AE394	RESPIRATORY FAILURE -ASTHMA	NEED FOR MECHANICAL VENTILATION REQUIRED GREATER THAN 24 HRS AFTER OF COMPLETION OF THE INDEX PROCEDURE (TIME 0 = WHEN THE SUBJECT LEAVES THE OR), OR NEED FOR RE-INTUBATION AND VENTILATOR SUPPORT OCCURRING ANY TIME WITHIN 30 DAY OF THE INDEX PROCEDURE WILL BE CONSIDERED RELATED TO THE INDEX PROCEDURE.
AE395	RESPIRATORY FAILURE -EMPHYSEMA	"
AE396	RESPIRATORY FAILURE -COPD	"
AE397	RESPIRATORY FAILURE -PNEUMONIA	"
AE398	RESPIRATORY FAILURE -PNEUMOTHORAX	"
AE399	RESPIRATORY FAILURE -HEMOTHORAX	"
AE400	RESPIRATORY FAILURE - ARDS	" ACUTE RESPIRATORY DISTRESS SYNDROME
AE401	RESPIRATORY FAILURE -OTHER	"
AE402	RESPIRATORY INFECTION – UPPER (URI)	THE ILLNESSES CAUSED BY AN ACUTE INFECTION WHICH INVOLVES THE UPPER RESPIRATORY TRACT: NOSE, SINUSES, PHARYNX OR LARYNX. THIS COMMONLY INCLUDES: TONSILLITIS, PHARYNGITIS, LARYNGITIS, SINUSITIS, OTITIS MEDIA, AND THE COMMON COLD.
AE403	RESPIRATORY INFECTION – PNEUMONIA	LUNG INFECTION DOCUMENTED BY BLOOD STUDIES OR CHEST X-RAY, REQUIRING TREATMENT WITH ANTIBIOTICS, INHALATION THERAPY, INTUBATION OR SUCTIONING.
AE.11	**PERIPHERAL VASCULAR**	
AE420	VASCULAR - ACCESS SITE COMPLICATION	COMPLICATIONS OF BLEEDING OR INFECTION AT THE SITE OF CARDIOPULMONARY ACCESS AND OR PERCUTANEOUS CORONARY INTERVENTION OR DIAGNOSTICS THAT REQUIRE HOSPITALIZATION OR MEDICAL INTERVENTION.
AE421	VASCULAR - DEEP VEIN THROMBOSIS (DVT)	FORMATION OF BLOOD CLOT (THROMBUS) IN THE LOWER EXTREMITIES (LEGS) CHARACTERIZED BY SWELLING, REDNESS, CLAUDICATION/PAIN IN AFFECTED LIMB. EVENT SHOULD BE CONFIRMED BY DOPPLER OR DUPLEX US STUDY, AND REQUIRES HOSPITALIZATION OR MEDICAL INTERVENTION TO RESOLVE.
AE423	VASCULAR - OTHER	OTHER VASCULAR COMPLICATIONS GENERALLY RELATED TO A DISEASE PROCESS AND NOT TRAUMA THAT REQUIRE HOSPITALIZATION OR MEDICAL INTERVENTION.
AE.12	**PSYCHIATRIC**	
AE431	PSYCHIATRIC DISORDER	A PSYCHOLOGICAL OR BEHAVIORAL PATTERN GENERALLY ASSOCIATED WITH SUBJECTIVE DISTRESS OR DISABILITY THAT OCCURS IN AN INDIVIDUAL, AND WHICH IS NOT A PART OF NORMAL DEVELOPMENT OR CULTURE. SUCH A DISORDER MAY CONSIST OF A COMBINATION OF AFFECTIVE, BEHAVIORAL, COGNITIVE AND PERCEPTUAL COMPONENTS.
AE432	SUICIDE	A PERSON WHO INTENTIONALLY TAKES HIS OR HER OWN LIFE.
AE433	TRANSIENT PSYCHOTIC SYNDROME	A MENTAL STATE OFTEN DESCRIBED AS INVOLVING A "LOSS OF CONTACT WITH REALITY" THAT LASTS ONLY FOR A SHORT TIME.
AE.12	**PSYCHIATRIC *(CONTINUED)***	

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE434	PSYCHIATRIC – OTHER	OTHER NEUROLOGIC EVENT NOT PREVIOUSLY DESCRIBED THAT REQUIRES HOSPITALIZATION OR MEDICAL INTERVENTION.
AE.13	**MUSCULAR SKELETAL/ DERMATOLOGIC**	
AE450	STERNAL WOUND/THORACIC INFECTION	DEEP STERNAL INFECTION INVOLVING MUSCLE, BONE, AND/OR MEDIASTINUM. MUST INCLUDE ONE OF THE FOLLOWING: 1) WOUND OPENED WITH EXCISION OF TISSUE (I&D); 2) POSITIVE CULTURE; 3) TREATMENT WITH ANTIBIOTICS. (LAST SENTENCE REMOVED, WHICH IMPLIES THAT BACTERIAL PNEUMONIA AFFECTING PARTS OF THE LUNG ADJACENT TO THE STERNUM SHOULD BE COUNTED AS A STERNAL WOUND INFECTION.)
AE451	BONE FRACTURE/BREAK	A BREAK IN BONE OR CARTILAGE. ALTHOUGH USUALLY THE RESULT OF TRAUMA, A FRACTURE CAN BE CAUSED BY AN ACQUIRED DISEASE OF BONE SUCH AS OSTEOPOROSIS OR BY ABNORMAL FORMATION OF BONE IN A DISEASE.
AE452	WOUND INFECTION – OTHER	OTHER WOUND INFECTION THAT IS NOT RELATED TO THE SURGICAL ACCESS SITE.
AE454	INFECTION /INFLAMMATION - OTHER	SOURCE OF INFECTION THAT IS CHARACTERIZED BY ELEVATED BLOOD LEVELS AND OR FEVER REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION (FEVER OF UNKNOWN ORIGIN FUO; CLINICALLY SIGNIFICANT ELEVATED WBC)
AE456	MUSCULAR SKELETAL / DERMATOLOGIC - OTHER	OTHER SKIN/MUSCULAR/SKELETAL EVENT NOT PREVIOUSLY DESCRIBED THAT REQUIRES HOSPITALIZATION OR MEDICAL INTERVENTION.
AE.14	**NONSPECIFIC, UNKNOWN, OR OTHER BODY SYSTEM**	
AE470	ANAPHYLACTIC REACTION	AN ALLERGIC REACTION TO AN ANTIGEN THAT CAUSES CIRCULATORY COLLAPSE AND SUFFOCATION DUE TO BRONCHIAL AND TRACHEAL SWELLING.
AE471	ALLERGIC REACTION – MEDICATION RELATED	A MILD TO MODERATE TO LIFE THREATENING REACTION TO A SUBSTANCE AND/OR MEDICATION. REPORT REACTIONS THAT REQUIRE HOSPITALIZATION OR MEDICAL INTERVENTION.
AE472	ALLERGIC REACTION – OTHER	A MILD TO MODERATE TO LIFE-THREATENING REACTION TO AN ENVIRONMENTAL OR ANIMAL SUBSTANCE. REPORT REACTIONS THAT REQUIRE HOSPITALIZATION OR MEDICAL INTERVENTION.
AE473	CANCER – PROGRESSION OF UNDERLYING DISEASE	AN EXACERBATION OR WORSENING OF A CANCER DIAGNOSED/KNOWN PRIOR TO THE INDEX PROCEDURE.
AE474	CANCER – NEWLY DIAGNOSED	A NEWLY DIAGNOSED CANCER FOLLOWING INDEX PROCEDURE.
AE475	HEARING DISORDER	ANY DISORDER RELATED TO HEARING IMPAIRMENT REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE476	MULTI-SYSTEM ORGAN FAILURE	OCCURS WHEN MORE THAN ONE ORGAN OF THE BODY STOPS FUNCTIONING NORMALLY AND HOMEOSTASIS CANNOT BE MAINTAINED WITHOUT INTERVENTION.
AE477	SPEECH DISORDER	ANY DISORDER RELATED TO A SPEECH IMPEDIMENT REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE479	VISION DISORDER	ANY DISORDER RELATED TO VISION IMPAIRMENT REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE480	FEVER - UNKNOWN ORIGIN	(1) A TEMPERATURE GREATER THAN 38.3°C (101°F) ON SEVERAL OCCASIONS, (2) MORE THAN 3 WEEKS' DURATION OF ILLNESS, AND (3) FAILURE TO REACH A DIAGNOSIS DESPITE 1 WEEK OF INSUBJECT INVESTIGATION.
AE481	NONSPECIFIC, UNKNOWN, OR OTHER BODY SYSTEM - OTHER COMPLICATION	ANY COMPLICATION THAT CANNOT OTHERWISE BE CATEGORIZED REQUIRING HOSPITALIZATION OR MEDICAL INTERVENTION.
AE.15	**DEVICE DYSFUNCTION**	

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE500	SVD - STUDY VALVE WEAR	INCLUDES DYSFUNCTION OR DETERIORATION INVOLVING THE OPERATED VALVE (EXCLUSIVE OF INFECTION OR THROMBOSIS). THE TERM STRUCTURAL VALVE DETERIORATION REFERS TO CHANGES INTRINSIC TO THE VALVE SUCH AS: WEAR, FRACTURE, CALCIFICATION, LEAFLET TEAR, MANUFACTURED SUTURE LINE DISRUPTION
AE501	SVD - STUDY VALVE FRACTURE	"
AE502	SVD - STUDY VALVE POPPET ESCAPE	"
AE503	SVD - STUDY VALVE CALCIFICATION	"
AE504	SVD - STUDY VALVE LEAFLET TEAR	"
AE505	SVD - STUDY VALVE STENT CREEP	"
AE506	SVD - STUDY VALVE SUTURE LINE DISRUPTION	"
AE507	SVD - STRUCTURAL VALVE DETERIORATION, OTHER	"
AE508	SVD - REPAIRED VALVE, NEW CHORDAL RUPTURE	
AE509	SVD - REPAIRED VALVE, LEAFLET DISRUPTION	
AE510	SVD - REPAIRED VALVE, LEAFLET RETRACTION	
AE511	SVD- REPAIRED VALVE, OTHER	
AE525	SVD - ANNULAR FRAME DAMAGE	"
AE526	SVD - ANNULAR FRAME SEPARATION	"
AE527	SVD - STENT FRAME FRACTURE	"
AE528	SVD - STENT FRAME DEFORMATION	"
AE529	SVD - STENT FRAME SEPARATION	"
AE512	NSD - ENTRAPMENT BY PANNUS, TISSUE, OR SUTURE	ANY ABNORMALITY NOT INTRINSIC TO THE VALVE (DO NOT DIRECTLY INVOLVE VALVE COMPONENTS) ITSELF THAT RESULTS IN STENOSIS OR REGURGITATION OF THE OPERATED VALVE OR HEMOLYSIS (EXCLUDES THROMBOSIS AND INFECTION). EXAMPLES INCLUDE: ENTRAPMENT BY PANNUS, TISSUE, OR SUTURE, PARAVALVULAR LEAK, INAPPROPRIATE SIZING, INAPPROPRIATE POSITIONING, REGURGITATION AS A RESULT OF TECHNICAL ERROR, STJ DILATION, DILATION OF THE VALVE ANNULUS, OBSTRUCTION OF THE CORONARY OSTIA BY THE STUDY VALVE.
AE164	NSD - PARAVALVULAR LEAK - +1	LEAKAGE BETWEEN THE SEWING RING AND THE ANNULUS.
AE165	NSD - PARAVALVULAR LEAK - +2	"
AE166	NSD - PARAVALVULAR LEAK - +3	"
AE167	NSD - PARAVALVULAR LEAK - +4	"
AE176	NSD - STUDY VALVE STENOSIS - MILD	NSD "

AE CODE LIST		
CODE	**LABEL/NAME**	**DEFINITION**
AE177	NSD - STUDY VALVE STENOSIS - MODERATE	NSD "
AE178	NSD - STUDY VALVE STENOSIS - SEVERE	NSD "
AE121	NSD - PARAVALVULAR LEAK WITH HEMOLYSIS	NSD "
AE514	NSD - INAPPROPRIATE SIZING	NSD "
AE516	NSD - RESIDUAL LEAK OR OBSTRUCTION	NSD "
AE517	NSD - INTRAVASCULAR HEMOLYTIC ANEMIA	NSD " CLINICALLY IMPORTANT
AE518	NSD - DEVELOPMENT OF REGURGITATION	NSD " AS A RESULT OF TECHNICAL ERRORS
AE519	NSD - DILATATION OF THE SINOTUBULAR JUNCTION	NSD "
AE520	NSD - DILATION OF THE VALVE ANNULUS	NSD "
AE521	NSD - CORONARY OSTIAL OBSTRUCTION	NSD "
AE522	NSD - STUDY VALVE INSTABILITY	NSD "
AE524	NSD - LVOT DAMAGE	NSD "
AE530	NSD - VALVE MALPOSITION	NSD "
AE531	NSD - VALVE MIGRATION/EMBOLIZATION	NSD "
AE532	NSD - VALVE DISLODGEMENT	NSD "

ATTACHMENT J – RESPONSIBILITIES

INVESTIGATOR & SPONSOR

INVESTIGATORS' RESPONSIBILITIES

1.0 Investigators' Responsibilities For Significant Risk Device Investigations (Nov. 1995)

This document is intended to assist investigators in identifying and complying with their responsibilities in connection with the conduct of clinical investigations involving medical devices. Although this guidance primarily addresses duties imposed upon clinical investigators by regulations of the Food and Drug Administration (FDA), investigators should be cognizant of additional responsibilities that may derive from other sources (such as the study protocol itself, the investigator agreement, any conditions of approval imposed by FDA or the governing Institutional Review Board, as well as institutional policy and state law).

2.0 General Responsibilities of Investigators (21 CFR 812.100)

- Ensuring that the investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations.
- Protecting the rights, safety, and welfare of subjects under the investigator's care.
- Controlling devices under investigation.
- Ensuring that informed consent is obtained from each subject in accordance with 21 CFR Part 50, and that the study is not commenced until FDA and IRB approvals have been obtained.

3.0 Specific Responsibilities of Investigators (21 CFR 812.110)

- Awaiting IRB approval and any necessary FDA approval before requesting written informed consent or permitting subject participation.
- Conducting the investigation in accordance with:
    - the signed agreement with the sponsor
    - the investigational plan
    - the regulations set forth in 21 CFR Part 812 and all other applicable FDA regulations
    - any conditions of approval imposed by an IRB or FDA
- Supervising the use of the investigational device. An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized under 21 CFR Part 812 to receive it.
- Disposing of the device properly. Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

4.0 Maintaining Records (21 CFR 812.140)

An investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

- Correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA.
- Records of receipt, use or disposition of a device that relate to:
    - the type and quantity of the device, dates of receipt, and batch numbers or code marks
    - names of all persons who received, used, or disposed of each device
    - the number of units of the device returned to the sponsor, repaired, or otherwise disposed of, and the reason(s) therefore
- Records of each subject's case history and exposure to the device, including:
    - documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent
    - all relevant observations, including records concerning adverse device effects (whether anticipated or not), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests
    - a record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy
- The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

5.0 Inspections (21 CFR 812.145)

Investigators are required to permit FDA to inspect and copy any records pertaining to the investigation including, in certain situations, those which identify subjects.

6.0 Submitting Reports (21 CFR 812.150)

An investigator shall prepare and submit the following complete, accurate, and timely reports:

- To the sponsor and the IRB:
  - Any unanticipated adverse device effect occurring during an investigation. (Due no later than 10 working days after the investigator first learns of the effect.)
  - Progress reports on the investigation. (These reports must be provided at regular intervals, but in no event less often than yearly. If there is a study monitor, a copy of the report should also be sent to the monitor.)
  - Any deviation from the investigational plan made to protect the life or physical well-being of a subject in an emergency. (Report is due as soon as possible but no later than 5 working days after the emergency occurs. Except in emergency situations, a protocol deviation requires prior sponsor approval; and if the deviation may affect the scientific soundness of the plan or the rights, safety, or welfare of subjects, prior FDA and IRB approval are required.)
  - Any use of the device without obtaining informed consent. (Due within 5 working days after such use.)
  - A final report. (Due within 3 months following termination or completion of the investigation or the investigator's part of the investigation. For additional guidance, see the discussion under the section entitled "Annual Progress Reports and Final Reports.")
  - Any further information requested by FDA or the IRB about any aspect of the investigation.
- To the Sponsor: Withdrawal of IRB approval of the investigator's part of an investigation. (Due within 5 working days of such action)

7.0 Investigational Device Distribution and Tracking

The IDE regulations prohibit an investigator from providing an investigational device to any person not authorized to receive it [21 CFR 812.110(c)]. The best strategy for reducing the risk that an investigational device could be improperly dispensed (whether purposely or inadvertently) is for the sponsor and the investigators to closely monitor the shipping, use, and final disposal of the device(s). Upon completion or termination of a clinical investigation (or the investigator's part of an investigation), or at the sponsor's request, an investigator is required to return to the sponsor any remaining supply of the device or otherwise to dispose of the device as the sponsor directs [21 CFR 812.110(c)]. Investigators must also maintain complete, current and accurate records of the receipt, use, or disposition of investigational devices [21 CFR 812.140(a)(2)]. Specific recordkeeping requirements are set forth at 21 CFR 812.140(a).

8.0 Prohibition of Promotion and Other Practices (21 CFR 812.7)

The IDE regulations prohibit the promotion and commercialization of a device that has not been first cleared or approved for marketing by FDA. This prohibition is applicable to sponsors and investigators (or any person acting on behalf of a sponsor or investigator), and encompasses the following activities:

- Promotion or test marketing of the investigational device
- Charging subjects or investigators for the device a price larger than is necessary to recover the costs of manufacture, research, development, and handling
- Prolonging an investigation beyond the point needed to collect data required to determine whether the device is safe and effective
- Representing that the device is safe or effective for the purposes for which it is being investigated.

SPONSOR'S RESPONSIBILITIES

1.0 Sponsor's Responsibilities For Significant Risk Device Investigations (Nov. 1995)

This document is intended to assist sponsors in identifying and complying with their responsibilities in connection with the conduct of clinical investigations of medical devices that are deemed "significant risk" by the reviewing IRB or by FDA. For a complete description of their responsibilities, sponsors should refer to the actual text of the regulations cited below. In addition, sponsors should be aware that a clinical investigation must be conducted in accordance with any requirements imposed by the reviewing IRB, by institutional policies, or by state law.

2.0 General Duties (21 CFR 812.40)

- Submitting the IDE application to FDA
- Obtaining both FDA and IRB approvals for the investigation and submitting certification of IRB approval to FDA before shipping the device to any investigator
- Obtaining FDA approval and IRB approval for a supplemental application before beginning that portion of the investigation
- Selecting qualified investigators
- Ensuring proper monitoring
- Ensuring patient informed consent is obtained

3.0 Selection of Investigators (21 CFR 812.43)

- Assuring selection of investigators qualified by training and experience
- Shipping the investigational device only to participating investigators
- Obtaining a signed investigator's agreement containing:
  - investigator's curriculum vitae
  - statement of investigator's relevant experience, including dates
  - location, extent, and type of experience
  - if an investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to the termination
  - statement of the investigator's commitment to:
    - conduct the investigation in accordance with the agreement, the investigational plan, Parts 50, 56, and 812, and any conditions of approval imposed by the IRB or FDA
    - supervise all testing of the device involving human subjects
    - ensure that the requirements for informed consent are met (21 CFR Part 50)
  - Providing investigators with the necessary information to conduct the investigation including, but not necessarily limited to:
  - the investigational plan
  - the report of prior investigations

4.0 Monitoring (21 CFR 812.46)

- Selecting monitor(s) qualified by training and experience to monitor the progress of the investigation
- Securing compliance of all investigators in accordance with the signed investigator's agreement, the investigational plan, the requirements of this part or other applicable FDA regulations, or any condition of approval imposed by the reviewing IRB or FDA. If compliance cannot be secured, shipment of the device to the investigator and the investigator's participation in the investigation must be discontinued
- Ensuring that significant new information about the investigation is provided to all reviewing IRBs, FDA, and investigators
- Evaluating all unanticipated adverse device effects and terminating the investigation, or portions of it, if that effect presents an unreasonable risk to subjects (reporting requirements are listed below.)
- Resuming terminated investigations only after both FDA and IRB approvals are obtained.

5.0 Controlling Distribution and Disposition of Devices

Although investigators are responsible for ensuring that investigational devices are made available only to persons who are legally authorized to receive them (*see* 21 CFR 812.110(c)), sponsors also bear responsibility for taking proper measures to ensure that devices are not diverted outside of legally authorized channels. Sponsors may ship investigational devices only to qualified investigators participating in the clinical investigation (§ 812.43(b)). Sponsors must also maintain complete, current, and accurate records pertaining to

the shipment and disposition of the investigational device (§ 812.140(b)). Records of shipment shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Records of disposition shall describe the batch number or code marks of any devices returned to the sponsor, repaired, or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.

To further ensure compliance with these requirements, sponsors should take appropriate measures to instruct investigators regarding their responsibilities with respect to recordkeeping and device disposition. The specific recordkeeping requirements for investigators are set forth at § 812.140(a). Upon completion or termination of a clinical investigation (or the investigator's part of an investigation), or at the sponsor's request, an investigator is required to return to the sponsor any remaining supply of the device or otherwise to dispose of the device as the sponsor directs (§ 812.110(c)).

6.0 Prohibition of Promotion and Other Practices (21 CFR 812.7)

The IDE regulations prohibit the promotion and commercialization of a device that has not been first cleared or approved for marketing by FDA. This prohibition is applicable to sponsors and investigators (or any person acting on behalf of a sponsor or investigator), and encompasses the following activities:

- Promotion or test marketing of the investigational device
- Charging subjects or investigators for the device a price larger than is necessary to recover the costs of manufacture, research, development, and handling
- Prolonging an investigation beyond the point needed to collect data required to determine whether the device is safe and effective
- Representing that the device is safe or effective for the purposes for which it is being investigated.

7.0 Supplemental Applications [21 CFR 812.35(a) and (b)]

Supplemental applications are required to be submitted to, and approved by, FDA in the following situations:

- **Changes in the investigational plan:** FDA approval is required for any change that may affect the scientific soundness of the investigation or the rights, safety or welfare of the subjects. IRB approval is also required for changes that may affect the rights, safety or welfare of the subjects. The change in the investigational plan may not be implemented until FDA approval (and IRB approval, if required) is obtained.
- **Addition of new institutions:** IRB approval is also required for new institutions. The investigation at the new institution(s) may not begin until both FDA and IRB approval(s) are obtained, and certification of IRB approval is submitted to FDA.

8.0 Maintaining Records [21 CFR 812.140(b)]

A sponsor shall maintain the following accurate, complete, and current records relating to an investigation (also *See* Table I, next page):

- Correspondence (including reports) with another sponsor, monitor, investigators, an IRB or FDA
- Records of shipment, including:
  - name and address of consignee
  - type and quantity of device
  - date of shipment
  - batch numbers or code marks
- Records of disposition, describing:
  - Batch number or code mark of devices returned, repaired, or disposed of by the investigator or other persons
  - Reasons for and method of disposal
- Signed investigator agreements
- Adverse device effects (whether anticipated or unanticipated) and complaints
- Any other records that FDA requires by regulation or by specific requirement for a category of investigation or a particular investigation

Table I Responsibilities for Maintaining Records for a Significant Risk Device Study

Records	Maintained by Investigator	Maintained by Sponsor
All Correspondence Pertaining to the Investigation	X	X
Shipment, Receipt, Disposition	X	X
Device Administration and Use	X	-
Subject Case Histories	X	-
Informed Consent	X	-
Protocols and Reasons for Deviations from Protocol	X	-
Adverse Device Effects and Complaints	X	X
Signed Investigator Agreements	-	X
Membership/Employment/Conflicts of Interest	-	X
Minutes of Meetings	-	-

9.0 Submitting Reports [21 CFR 812.150(b)]

A sponsor shall prepare and submit the following complete, accurate, and timely reports (see Table II).

- Unanticipated adverse device effects (with evaluation) to FDA, all IRBs, and investigators within 10 working days after notification by the investigator. Subsequent reports on the effect may be required by FDA.
- Withdrawal of IRB approval
- Withdrawal of FDA approval
- Current 6month investigator list
- Annual progress report see format for IDE progress report
- Recall and device disposition (within 30 working days after the request was made)
- Final report see format for progress reports
- Use of device without obtaining patient informed consent
- Significant risk determinations by the IRB when proposed to be non-significant risk
- Other reports requested by the IRB or FDA

Table II Responsibilities for Preparing and Submitting Reports for Significant Risk Device Studies

Type of Report	Prepared by Investigators for	Prepared by Sponsors for
Unanticipated Adverse Effect Evaluation	Sponsors & IRBs	FDA, IRBs & Investigators
Withdrawal of IDE Approval	Sponsors	FDA, IRBs, & Investigators
Progress Report	Sponsors, Monitors & IRBs	FDA & IRBs
Final Report	Sponsors & IRBs	FDA, IRBs, & Investigators
Emergencies (Protocol Deviations)	Sponsors & IRBs	FDA
Inability to Obtain Informed Consent	Sponsors & IRBs	FDA
Withdrawal of FDA Approval	N/A	IRBs & Investigators
Current Investigator List	N/A	FDA
Recall and Device Disposition	< N/A	FDA & IRBs
Records Maintenance Transfer	FDA	FDA
Significant Risk Determinations	N/A	FDA

10.0 Inspections [21 CFR 812.145]

Sponsors are required to permit FDA to enter and inspect (at reasonable times and in a reasonable manner) any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records or results from use of devices are kept). FDA may also inspect and copy all records relating to an investigation including, in certain situations, records which, identify subjects.

ATTACHMENT K – SUBJECT IMPLANT CARD

Outside of Card

MR Conditional

Non-clinical testing has demonstrated that the Edwards Aortic Bioprosthesis, Model 11000A, is MR Conditional. A patient with the Model 11000A valve can be scanned safely, immediately after placement of this implant under the following conditions:
- Static magnetic field of 1.5 tesla or 3.0 tesla.
- Maximum spatial magnetic gradient field of 2670 gauss/cm.
- Maximum MR system-reported whole-body averaged specific absorption rate (SAR) of 2.0 W/kg in the normal operating mode for 15 minutes of scanning per sequence.

In non-clinical testing, the Edwards Aortic Bioprosthesis, Model 11000A, produced an estimated maximum *in vivo* temperature rise of less than or equal to 1.8 °C at a maximum MR system-reported, whole-body averaged specific absorption rate (SAR) of 2.0 W/kg, for 15 minutes of MR scanning in a GE Signa 64 MHz (1.5T) RF coil and a GE Signa HDx (3T) MR system with Software Version 15\LX\MR Software release 15.0.M4.0910.a.

Image artifact was measured non-clinically in a GE Signa 3T HDx MR System according to ASTM F2119-07 using the spin echo and gradient echo sequences specified therein. The spin echo images exhibited light and dark artifacts that extended as far as 40 mm from the implant and partially to fully obscured the lumen. The gradient echo images exhibited opaque dark or light and dark triangular shaped artifacts that extended as far as 40 mm from the implant and totally obscured the lumen. Reduction in artifact may be possible with sequences designed for reduction of metal artifact.

Tel (USA) 800.424.3278 Tel (outside USA) +1.949.250.2500

Subject ID 2012-02-_____

Trial Site Physician _____

Physician Contact # _____

Hospital _____

Date: ____/____/____ (Month Day Year)

EDWARDS Pericardial Aortic Bioprosthesis Model 11000A

Edwards Lifesciences

Back
(to have MR statement for USA)

Front

Inside of Card

The following aortic valve was implanted.

Please affix the self-adhesive label with the serial number for the aortic valve implanted in this patient. This label may be found in the original device package.

IMPORTANT: **For all other questions or concerns, contact:**

Physician Name Contact Number

Follow-Up Schedule

1 Month: _____/_____ (Month Year) ☐ Office visit ☐ Telephone interview

3 Month: _____/_____ (Month Year)

1 year: _____/_____ (Month Year)

2 year: _____/_____ (Month Year)

3 year: _____/_____ (Month Year)

4 year: _____/_____ (Month Year)

5 year: _____/_____ (Month Year)

Outside of Card

MR Conditional

Non-clinical testing has demonstrated that the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is MR Conditional. A patient with the Model 11000M bioprosthesis can be scanned safely, immediately after placement of this implant under the following conditions:
- Static magnetic field of 3 tesla or less.
- Maximum Spatial gradient field of 720 gauss/cm.
- Maximum MR system-reported whole-body-averaged specific absorption rate (SAR) of 3W/kg for 15 minutes of scanning.

In non-clinical testing, the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, produced a temperature rise of less than or equal to 0.5 °C at a maximum MR system reported whole-body-averaged specific absorption rate (SAR) of 3W/kg for 15 minutes of MR scanning in a 3 tesla MR system (Excite, Software G3.0-052B, General Electric Healthcare).

MR image quality may be compromised if the area of interest is in the same area or relatively close to the position of the Model 11000M bioprosthesis. Optimization of MR imaging parameters is recommended.

Tel (USA) 800.424.3278 Tel (outside USA) +1.949.250.2500

Back
(to have MR statement for USA)

Subject ID 2012-02-_____

Trial Site Physician _____

Physician Contact # _____

Hospital _____

Date: ____/____/____ (Month Day Year)

EDWARDS Pericardial Mitral Bioprosthesis Model 11000M

Edwards Lifesciences

Front

Inside of Card

The following mitral valve was implanted.

Please affix the self-adhesive label with the serial number for the mitral valve implanted in this patient. This label may be found in the original device package.

IMPORTANT: **For all other questions or concerns, contact:**

Physician Name Contact Number

Follow-Up Schedule

1 Month: _____/_____ (Month Year) ☐ Office visit ☐ Telephone interview

3 Month: _____/_____ (Month Year)

1 year: _____/_____ (Month Year)

2 year: _____/_____ (Month Year)

3 year: _____/_____ (Month Year)

4 year: _____/_____ (Month Year)

5 year: _____/_____ (Month Year)

ATTACHMENT L – PROTOCOL DEVIATION CODES

PROTOCOL DEVIATION CODES

SUBJECT SCREENING

1.01 SUBJECT DID NOT MEET INCLUSION CRITERION
1.02 SUBJECT MET EXCLUSION CRITERION
1.03 DATE OF INFORMED CONSENT IS AFTER DATE OF STUDY ENROLLMENT
1.04 INFORMED CONSENT WAS IMPROPERLY OBTAINED
1.05 PERSON OBTAINING INFORMED CONSENT DID NOT SIGN/DATE THE CONSENT FORM
1.06 OTHER SCREENING DEVIATION

BASELINE

2.01 BASELINE ECHOCARDIOGRAM NOT DONE
2.21 BASELINE ECHOCARDIOGRAM DONE > 60 DAYS PRIOR IMPLANT DATE
2.03 BASELINE BLOOD NOT DONE
2.22 BASELINE BLOOD DONE > 60 DAYS BEFORE IMPLANT
2.05 BASELINE BLOOD INCOMPLETE
2.06 BASELINE COAGULATION PROFILE NOT DONE
2.23 BASELINE COAGULATION PROFILE DONE > 60 DAYS BEFORE IMPLANT
2.08 BASELINE NYHA NOT DONE
2.09 BASELINE ELECTROCARDIOGRAM NOT DONE
2.24 BASELINE ELECTROCARDIOGRAM DONE > 60 DAYS BEFORE IMPLANT
2.11 BASELINE PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
2.12 PREGNACY TEST NOT DONE
2.13 MEDICAL HISTORY NOT COLLECTED
2.10 BASELINE QUALITY OF LIFE NOT DONE
2.14 OTHER BASELINE DEVIATION

IMPLANT SURGERY

3.01 IMPLANTING SURGEON IS NOT ON APPROVED LIST
3.02 PROCEDURE DIAGNOSIS NOT DONE
3.28 INCORRECT SIZER USED
3.04 START SKIN INCISION TIME NOT RECORDED
3.05 START TIME OF ECC (PUMP) NOT RECORDED
3.06 START CROSS CLAMP TIME NOT RECORDED
3.07 START OF SIZING TIME NOT RECORDED
3.09 REMOVAL CROSS CLAMP TIME NOT RECORDED
3.10 END ECC (PUMP) TIME NOT RECORDED
3.11 END SKIN CLOSURE TIME NOT RECORDED
3.12 UNAPPROVED CONCOMITANT PROCEDURE PERFORMED
3.15 VALVE SERIAL NUMBER NOT RECORDED
3.18 MORE THAN 2 STUDY VALVES ATTEMPTED TO BE IMPLANTED
3.21 START TIME FOR STUDY PROCEDURE (FIST STITCH PLACED ON THE ANNULUS) NOT RECORDED
3.22 TIME FIST STITCH PLACED ON THE VALVE RING NOT RECORDED

3.26 COMPLETION TIME OF STUDY PROCEDURE (LAST STITCH TIED DOWN ON THE VALVE) NOT RECORDED
3.33 POST-IMPLANT ECHOCARDIOGRAM NOT DONE
3.30 POST-IMPLANT ECHOCARDIOGRAM NOT DONE WITHIN 1 HOUR OF REMOVING THE CROSS-CLAMP
3.31 PRE-IMPLANT BLOOD COLLECTION (SERUM GLYCEROL) NOT DONE (ONLY REQUIRED FOR 120 SUBJECTS)
3.19 POST-IMPLANT BLOOD COLLECTION (SERUM GLYCEROL) NOT DONE (ONLY REQUIRED FOR 120 SUBJECTS)
3.32 POST-IMPLANT BLOOD COLLECTION (SERUM GLYCEROL) NOT DONE WITHIN 120 MINUTES OF RESTARTING THE HEART (ONLY REQUIRED FOR 120 SUBJECTS)
3.27 OTHER PROCEDURE DEVIATION

DISCHARGE

4.01 DISCHARGE OR 10-DAY ECHOCARDIOGRAM NOT DONE
4.02 DISCHARGE OR 10-DAY ECHOCARDIOGRAM DONE > 10 DAYS POST IMPLANT DATE
4.03 DISCHARGE PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
4.04 DISCHARGE ELECTROCARDIOGRAM NOT DONE
4.05 DISCHARGE COAGULATION PROFILE NOT DONE
4.07 DISCHARGE MEDICATIONS NOT ASSESSED
4.09 DISCHARGE HOSPITALIZATION TIMES NOT COLLECTED
4.08 OTHER DISCHARGE DEVIATION

1 MONTH

5.01 1 MONTH- SUBJECT NOT CONTACTED
5.01 1 MONTH- MISSED VISIT- SUBJECT CONTACTED
5.02 1 MONTH- ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
5.03 1 MONTH - NYHA NOT DONE
5.04 1 MONTH - MEDICATIONS NOT ASSESSED
5.05 1 MONTH - OTHER DEVIATION

3 MONTH

6.01 3 MONTH - SUBJECT NOT CONTACTED
6.01 3 MONTH - MISSED VISIT- SUBJECT CONTACTED
6.02 3 MONTH - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
6.03 3 MONTH - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
6.04 3 MONTH - NYHA NOT DONE
6.05 3 MONTH - ELECTROCARDIOGRAM NOT DONE
6.06 3 MONTH - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
6.07 3 MONTH - ECHOCARDIOGRAM NOT DONE
6.08 3 MONTH - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
6.09 3 MONTH - BLOOD NOT DONE
6.10 3 MONTH - BLOOD INCOMPLETE
6.11 3 MONTH - COAGULATION PROFILE NOT DONE
6.12 3 MONTH - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
6.13 3 MONTH - MEDICATIONS NOT ASSESSED
6.14 3 MONTH - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
6.15 3 MONTH - OTHER DEVIATION

1 YEAR

8.01 1 YEAR - SUBJECT NOT CONTACTED
8.01 1 YEAR – MISSED VISIT- SUBJECT CONTACTED
8.02 1 YEAR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
8.03 1 YEAR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
8.04 1 YEAR - NYHA NOT DONE
8.05 1 YEAR - ELECTROCARDIOGRAM NOT DONE
8.06 1 YEAR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
8.07 1 YEAR - ECHOCARDIOGRAM NOT DONE
8.08 1 YEAR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
8.09 1 YEAR - BLOOD NOT DONE
8.10 1 YEAR - BLOOD INCOMPLETE
8.11 1 YEAR - COAGULATION PROFILE NOT DONE
8.12 1 YEAR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
8.13 1 YEAR - MEDICATIONS NOT ASSESSED
8.14 1 YEAR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
8.16 1 YEAR- QUALITY OF LIFE NOT DONE
8.15 1 YEAR - OTHER DEVIATION

2 YEAR

9.01 2 YEAR - SUBJECT NOT CONTACTED
9.01 2 YEAR –MISSED VISIT- SUBJECT CONTACTED
9.02 2 YEAR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
9.03 2 YEAR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
9.04 2 YEAR - NYHA NOT DONE
9.05 2 YEAR - ELECTROCARDIOGRAM NOT DONE
9.06 2 YEAR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
9.07 2 YEAR - ECHOCARDIOGRAM NOT DONE
9.08 2 YEAR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
9.09 2 YEAR - BLOOD NOT DONE
9.10 2 YEAR - BLOOD INCOMPLETE
9.11 2 YEAR - COAGULATION PROFILE NOT DONE
9.12 2 YEAR- BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
9.13 2 YEAR - MEDICATIONS NOT ASSESSED
9.14 2 YEAR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
9.15 2 YEAR - OTHER DEVIATION

3 YEAR

10.01 3 YEAR - SUBJECT NOT CONTACTED
10.01 3 YEAR – MISSED VISIT- SUBJECT CONTACTED
10.02 3 YEAR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
10.03 3 YEAR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
10.04 3 YEAR - NYHA NOT DONE
10.05 3 YEAR - ELECTROCARDIOGRAM NOT DONE
10.06 3 YEAR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
10.07 3 YEAR - ECHOCARDIOGRAM NOT DONE
10.08 3 YEAR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
10.09 3 YEAR - BLOOD NOT DONE
10.10 3 YEAR - BLOOD INCOMPLETE
10.11 3 YEAR - COAGULATION PROFILE NOT DONE
10.12 3 YEAR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
10.13 3 YEAR - MEDICATIONS NOT ASSESSED
10.14 3 YEAR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
10.15 3 YEAR - OTHER DEVIATION

4 YEAR

11.01 4 YEAR - SUBJECT NOT CONTACTED
11.01 4 YEAR – MISSED VISIT- SUBJECT CONTACTED
11.02 4 YEAR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
11.03 4 YEAR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
11.04 4 YEAR - NYHA NOT DONE
11.05 4 YEAR - ELECTROCARDIOGRAM NOT DONE
11.06 4 YEAR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
11.07 4 YEAR - ECHOCARDIOGRAM NOT DONE
11.08 4 YEAR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
11.09 4 YEAR - BLOOD NOT DONE
11.10 4 YEAR - BLOOD INCOMPLETE
11.11 4 YEAR - COAGULATION PROFILE NOT DONE
11.12 4 YEAR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
11.13 4 YEAR - MEDICATIONS NOT ASSESSED
11.14 4 YEAR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
11.15 4 YEAR - OTHER DEVIATION

5 YEAR

12.01 5 YEAR - SUBJECT NOT CONTACTED
12.01 5 YEAR – MISSED VISIT - SUBJECT CONTACTED
12.02 5 YEAR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
12.03 5 YEAR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
12.04 5 YEAR - NYHA NOT DONE
12.05 5 YEAR - ELECTROCARDIOGRAM NOT DONE
12.06 5 YEAR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
12.07 5 YEAR - ECHOCARDIOGRAM NOT DONE
12.08 5 YEAR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
12.09 5 YEAR - BLOOD NOT DONE
12.10 5 YEAR - BLOOD INCOMPLETE
12.11 5 YEAR - COAGULATION PROFILE NOT DONE
12.12 5 YEAR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
12.13 5 YEAR - MEDICATIONS NOT ASSESSED
12.14 5 YEAR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
12.15 5 YEAR - OTHER DEVIATION

6 year

16.01 6 YR - SUBJECT NOT CONTACTED
16.01 6 YR – MISSED VISIT - SUBJECT CONTACTED
16.02 6 YR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
16.03 6 YR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
16.04 6 YR - NYHA NOT DONE
16.05 6 YR - ELECTROCARDIOGRAM NOT DONE
16.06 6 YR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
16.07 6 YR - ECHOCARDIOGRAM NOT DONE
16.08 6 YR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
16.09 6 YR - BLOOD NOT DONE
16.10 6 YR - BLOOD INCOMPLETE
16.11 6 YR - COAGULATION PROFILE NOT DONE
16.12 6 YR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
16.13 6 YR - MEDICATIONS NOT ASSESSED
16.14 6 YR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
16.15 6 YR - OTHER DEVIATION

7 year

17.01	7 YR - SUBJECT NOT CONTACTED
17.01	7 YR – MISSED VISIT - SUBJECT CONTACTED
17.02	7 YR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
17.03	7 YR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
17.04	7 YR - NYHA NOT DONE
17.05	7 YR - ELECTROCARDIOGRAM NOT DONE
17.06	7 YR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
17.07	7 YR - ECHOCARDIOGRAM NOT DONE
17.08	7 YR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
17.09	7 YR - BLOOD NOT DONE
17.10	7 YR - BLOOD INCOMPLETE
17.11	7 YR - COAGULATION PROFILE NOT DONE
17.12	7 YR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
17.13	7 YR - MEDICATIONS NOT ASSESSED
17.14	7 YR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
17.15	7 YR - OTHER DEVIATION

8 year

18.01	8 YR - SUBJECT NOT CONTACTED
18.01	8 YR – MISSED VISIT - SUBJECT CONTACTED
18.02	8 YR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
18.03	8 YR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
18.04	8 YR - NYHA NOT DONE
18.05	8 YR - ELECTROCARDIOGRAM NOT DONE
18.06	8 YR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
18.07	8 YR - ECHOCARDIOGRAM NOT DONE
18.08	8 YR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
18.09	8 YR - BLOOD NOT DONE
18.10	8 YR - BLOOD INCOMPLETE
18.11	8 YR - COAGULATION PROFILE NOT DONE
18.12	8 YR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
18.13	8 YR - MEDICATIONS NOT ASSESSED
18.14	8 YR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
18.15	8 YR - OTHER DEVIATION

9 year

19.01 9 YR - SUBJECT NOT CONTACTED
19.01 9 YR – MISSED VISIT - SUBJECT CONTACTED
19.02 9 YR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
19.03 9 YR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
19.04 9 YR - NYHA NOT DONE
19.05 9 YR - ELECTROCARDIOGRAM NOT DONE
19.06 9 YR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
19.07 9 YR - ECHOCARDIOGRAM NOT DONE
19.08 9 YR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
19.09 9 YR - BLOOD NOT DONE
19.10 9 YR - BLOOD INCOMPLETE
19.11 9 YR - COAGULATION PROFILE NOT DONE
19.12 9 YR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
19.13 9 YR - MEDICATIONS NOT ASSESSED
19.14 9 YR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
19.15 9 YR - OTHER DEVIATION

10 year

20.01 10 YR - SUBJECT NOT CONTACTED
20.01 10 YR – MISSED VISIT - SUBJECT CONTACTED
20.02 10 YR - ASSESSMENT NOT DONE WITHIN FOLLOW-UP WINDOW
20.03 10 YR - PHYSICAL ASSESSMENT / VITAL SIGNS NOT DONE
20.04 10 YR - NYHA NOT DONE
20.05 10 YR - ELECTROCARDIOGRAM NOT DONE
20.06 10 YR - ELECTROCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
20.07 10 YR - ECHOCARDIOGRAM NOT DONE
20.08 10 YR - ECHOCARDIOGRAM NOT DONE WITHIN FOLLOW-UP WINDOW
20.09 10 YR - BLOOD NOT DONE
20.10 10 YR - BLOOD INCOMPLETE
20.11 10 YR - COAGULATION PROFILE NOT DONE
20.12 10 YR - BLOOD NOT DONE WITHIN FOLLOW-UP WINDOW
20.13 10 YR - MEDICATIONS NOT ASSESSED
20.14 10 YR - MEDICATIONS NOT ASSESSED WITHIN FOLLOW-UP WINDOW
20.15 10 YR - OTHER DEVIATION

Adverse Event

14.01 UADE NOT REPORTED WITHIN 10 WORKING DAYS OF THE INVESTIGATOR AWARENESS DATE
14.02 OTHER ADVERSE EVENT DEVIATION

Miscellaneous

15.01 STUDY DEVICE USED IN A SUBJECT NOT ENROLLED IN THE STUDY
15.02 OTHER DEVIATION

ATTACHMENT M – DEVICE DEFICIENCY CODES

DEVICE DEFICIENCY CODES

Code	Label
DD.2	**Valve / Holder**
DD.2.01	Device function, packaging not intact
DD.2.02	Device function, component contamination
DD.2.03	Device function, unable to remove from jar
DD.2.04	Device function, unable to place sutures through sewing ring
DD.2.05	Device function, unable to position on the annulus
DD.2.06	Device function, bioprosthesis and holder separate during procedure
DD.2.07	Device function, other, specify
DD.2.08	Device use, sizing technique
DD.2.09	Device use, sterility compromised
DD.2.10	Device use, used expired product
DD.2.11	Device use, component damaged by operator
DD.2.12	Device use, improper positioning
DD.2.13	Device use, other specify

ATTACHMENT N – CLINICAL TRIAL AGREEMENT

No Longer In Use

ATTACHMENT O – POWER SIMULATION CODE FOR PRIMARY SAFETY ENDPOINT

No Longer In Use