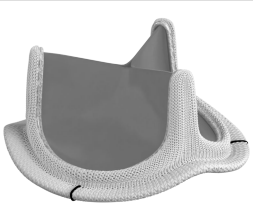
INSPIRIS RESILIA Aortic Valve, Model 11500A

Instructions for Use

Refer to Figures 1 through 11 on pages 12 and 13.



Model 11500A

1.0 Device and Accessories Description

1.1 Device Description

The INSPIRIS RESILIA aortic valve, model 11500A, is a stented trileaflet valve comprised of RESILIA bovine pericardial tissue that is mounted on a flexible frame. The valve is stored under dry packaging conditions and consequently does not require rinsing prior to implantation. The valve is available in sizes 19, 21, 23, 25, 27 and 29 mm. See Table 1 for nominal dimensions.

1.1.1 RESILIA Tissue

RESILIA tissue is created with a novel technology called Edwards Integrity Preservation. The technology incorporates a stable capping anticalcification process, which permanently blocks residual aldehyde groups that are known to bind with calcium. The technology also incorporates tissue preservation with glycerol, which replaces the traditional storage in liquid-based solutions such as glutaraldehyde. The storage method eliminates tissue exposure to the residual unbound aldehyde groups commonly found in glutaraldehyde storage solutions and maintains long-term protection of collagen.

The combined impact of the Edwards Integrity Preservation technology's stable capping and glycerolization features makes it a superior, resilient tissue. In juvenile sheep, valves with RESILIA tissue demonstrated a statistically significant reduction in leaflet calcification ($p = 0.002$) and significant improvement in hemodynamic performance ($p = 0.03$) over commercially available pericardial tissue valves (Carpentier-Edwards PERIMOUNT Plus pericardial mitral bioprosthesis, model 6900P) (Refs. 1 and 2). No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients. Additional clinical data for up to 10 years of follow-up are being collected to monitor the safety and performance of RESILIA tissue.

1.1.2 Valve Structure

The frame is designed to be compliant at the orifice as well as at the commissures. The compliance of the commissure supports is intended to reduce the loading shock at the valve commissures and free margin of the leaflets (Ref. 3). The compliance of the orifice is intended to reduce the stress on the leaflets.

The compliant orifice concept is based on the physiology and mechanics of natural heart valves and reported experience with implantation of unstented homografts (Refs. 4 and 5).

The lightweight wireform is made of a corrosion-resistant cobalt-chromium alloy, chosen because of its superior spring efficiency and fatigue-resistant characteristics, and is covered with a polyester fabric.

As in the Carpentier-Edwards PERIMOUNT Magna Ease aortic bioprosthesis, model 3300TFX a thin cobalt-chromium alloy band and polyester support band surround the base of the valve beneath the wireform frame providing structural support for the orifice.

In the INSPIRIS RESILIA aortic valve, the ends of the cobalt-chromium alloy band are secured by a polyester shrink sleeve on the sizes 19 – 25 mm to allow the internal orifice of the valve to expand. The polyester support band allows expansion at each commissure when subjected to radial forces.

Valves with expandable bands (sizes 19 – 25 mm) (Figure 1) will maintain a stable diameter at implant and under intracardiac conditions, which was demonstrated during compression resistance testing and accelerated wear testing.

In the sizes 27 and 29 mm, the free ends of the cobalt-chromium alloy band are permanently secured using a weld joint. Refer to Figures 3 through 5 for a comparison between the INSPIRIS RESILIA aortic valve and Carpentier-Edwards PERIMOUNT Magna Ease aortic bioprosthesis. A silicone rubber sewing ring that is covered with a porous, seamless polytetrafluoroethylene (PTFE) cloth is attached to the wireform frame and facilitates tissue ingrowth and encapsulation. The aortic sewing ring is scalloped to conform to the natural aortic root. The compliant nature of the sewing ring facilitates coaptation between the valve and an often irregular or calcific tissue bed.

To facilitate implantation in patients with small aortic roots, the model 11500A has a low profile height. The sewing ring has three equally spaced black silk suture markers at the cusp centers to aid in valve orientation and suture placement. Changes to the cobalt-chromium alloy band and polyester band do not impact suture placement or implant technique.

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

Similar to other Edwards bioprosthetic valves, the cobalt-chromium alloy wireform in the model 11500A, is easily identified on fluoroscopy. This allows for identification of the valve's inflow and outflow edges.

1.2 VFit Technology

VFit technology is available on the model 11500A sizes 19 – 25 mm. This technology incorporates two novel features designed for potential future valve-in-valve (ViV) procedures: fluoroscopically visible size markers and an expansion zone.

The fluoroscopically visible size marker is designed to aid the clinician in surgical valve size identification after implantation. A representation of the commissure size markers for the sizes 19 – 25 mm is shown in Figure 2.

WARNING: SIZE MARKER CORRESPONDS TO THE LABELED VALVE SIZE OF THE INSPIRIS RESILIA VALVE AND IS

NOT A REPLACEMENT FOR CURRENT SIZE IDENTIFICATION TECHNIQUES RECOMMENDED FOR USE IN TRANSCATHETER PROCEDURES. Variability of patient anatomy and imaging quality may impact visibility of size markers and lead to misidentification of valve size.

The expansion zone is designed to address increased mortality risk associated with ViV in smaller surgical valves (Ref. 6). To address these risks the expansion zone enables an increased band diameter and larger orifice for ViV procedure planning and implantation. Because a larger orifice area is generally associated with lower gradients (Ref. 7), the expansion zone may improve post-procedural ViV gradients compared to ViV in surgical valves that do not expand.

Activation of the expansion zone is achieved from the applied radial force of the transcatheter valve.

WARNING: Valve-in-valve sizing in the INSPIRIS RESILIA valve has only been tested with specific Edwards transcatheter heart valves. Use of other transcatheter valves may result in embolization of transcatheter devices anchored within or result in annular rupture.

Refer to the appropriate transcatheter valve instructions for use for proper sizing for valve- in-valve procedures.

Long term durability was not assessed as part of the ViV testing with the model 11500A. The impact of tissue ingrowth on the expansion feature of the valve has not been assessed. Expansion has not been assessed with self-expanding transcatheter heart valves. These findings have not been observed in clinical studies to establish the safety and effectiveness of the model 11500A for use in ViV procedures. Expansion has not demonstrated improved hemodynamic performance for ViV versus the model 3300TFX.

IMPORTANT WARNINGS RELATED TO BAND EXPANSION:

DO NOT PERFORM BALLOON AORTIC VALVULOPLASTY PROCEDURES ON THIS VALVE FOR THE SIZES 19 – 25 mm. Although the valve will maintain a stable diameter at implant and during intracardiac conditions, the diameter of this valve will expand if radial force is applied, such as during a balloon aortic valvuloplasty. This may expand the valve causing aortic incompetence.

DO NOT ADJUST THE VALVE DIAMETER USING THE EXPANSION ZONE DURING IMPLANTATION OF THE SURGICAL VALVE. The expansion zone is not designed to allow for compression or expansion during implantation of the surgical valve. Doing so will cause damage to the valve and may result in aortic incompetence.

1.3 Sizers and Tray

The use of a sizing instrument facilitates selection of the correct size valve 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 (See Figure 6). On one side of the handle is a cylindrical end with an integrated lip that reflects the valve sewing ring geometry. On the other side of the handle is a valve replica end that reflects the valve sewing ring geometry as well as the height and location of the stent posts. A sizer is available for each size of the model 11500A valve (19, 21, 23, 25, 27, and 29 mm). The complete set of sizers is housed in a tray, model TRAY1133.

1.4 Valve Holder and Handle

The model 11500A valve has an integrated disposable holder. A malleable handle (model 1111 or model 1126) is attached to the holder at the time of surgery.

The benefits of this device include improvement in aortic valve function and longevity, acute relief of symptoms, and improvement in morbidity and mortality.

2.0 Intended Use and Indications for Use

The INSPIRIS RESILIA aortic valve, model 11500A, is intended for use as a heart valve replacement.

The INSPIRIS RESILIA aortic valve, model 11500A, is indicated for patients who require replacement of their native or prosthetic aortic valve.

3.0 Contraindications

There are no known contraindications with the use of the INSPIRIS RESILIA aortic valve.

4.0 Warnings

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. Resterilization could lead to injury or infection, as the device may not function as intended.

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

DO NOT USE the valve if:

- **The foil pouch, sealed trays or lids are opened, damaged, or stained**
- **The expiration date has elapsed, or**
- **It is dropped, damaged, or mishandled in any way.**

The above may result in dehydration of the tissue, contamination, and/or compromised sterility.

Should a valve be damaged during insertion, do not attempt repair.

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

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

DO NOT PASS CATHETERS or transvenous pacing leads across the valve since they may cause tissue damage. Care must be exercised when passing a surgical instrument across the valve to avoid leaflet tissue damage.

As with any implanted medical device, there is a potential for the patient to develop an immunological response. Refer to Section 12.0 Qualitative and Quantitative Information for a listing of materials and substances in this device. Patients with hypersensitivities to cobalt, chromium, nickel, molybdenum, manganese, carbon, beryllium, iron, glycerol, and bovine tissue may have an allergic reaction to these materials. 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.

5.0 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 INSPIRIS RESILIA aortic valve, model 11500A is similar in design to the Carpentier-Edwards PERIMOUNT Magna Ease pericardial aortic bioprosthesis, 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 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.

5.2 Potential Adverse Events

Adverse events potentially associated with the use of valves and the surgical procedure include:

- Allergic reaction
- Angina
- Annulus (damage, dissection, tear)
- Arterial dissection
- Aorta (damage, dissection, tear)
- Aortic Root damage
- Asystole and/or cardiac arrest
- Bleeding
  - Peri- or post-procedural
  - Anticoagulant related
  - Pericardial tamponade
  - Hematoma
  - Cerebrovascular
- Blood - Anemia
- Blood - Coagulopathy
- Blood – Hemolysis/Hemolytic Anemia
- Blood Pressure alteration (hypotension, hypertension)
- Cardiac – Arrhythmias/Conduction Disturbances
- Cardiogenic shock
- Coronary artery ostia occlusion
- Deep vein thrombosis (DV)
- Disseminated intravascular coagulation (DIC)
- Embolism
- Endocarditis
- Esophageal tear/rupture
- Hypoxemia
- Infection – local, wound or systemic
- Multi-system organ failure (MOF)
- Myocardial infarction
- Neurologic Events
  - Stroke (CVA)
  - Transient Ischemic Attack (TIA)
- Pericardial effusion
- Pleural effusion
- Pneumonia
- Prosthetic Insufficiency –Regurgitation/Stenosis
- Pulmonary edema
- Reduced exercise tolerance
- Renal failure, acute
- Renal insufficiency
- Respiratory failure
- Thrombocytopenia (Non-HIT)
- Thrombocytopenia, heparin induced (HIT)
- Thromboembolism
  - Arterial, venous, peripheral, central
- Transvalvular or Valvular Leaking
- Valve dislodgement/instability
- Valve – Nonstructural dysfunction
  - Paravalvular Leak
  - Leaflet impingement
  - Leaflet tissue damage (instruments /sutures)
  - Pannus
  - Patient Prosthesis Mismatch (PPM) (due to inappropriate sizing)
  - Distortion at implant
- Valve - Structural dysfunction/deterioration
- Valve - Thrombosis
- Valve Wireform/Stent Fracture or Distortion

Calcific and non-calcific (fibrotic) degeneration of bioprosthetic valves is reported with use of chemo-radiotherapy to treat malignant conditions (Refs. 8 and 9).

It is possible that these complications may lead to:

- Reoperation
- Explantation
- Permanent disability
- Death

6.0 Clinical Studies

The clinical safety and effectiveness of the INSPIRIS RESILIA aortic valve, model 11500A was established based on the outcome data of the COMMENCE trial. The purpose of this study was to assess the safety and effectiveness of the RESILIA tissue, packaging and sterilization.

The COMMENCE trial is an open-label, prospective, non-randomized, multicenter trial without concurrent or matched controls. Following a pre-surgical assessment, subjects are followed for one year to assess primary safety and effectiveness. Subjects are followed annually thereafter for a minimum of five years post-surgical experience. Long-term follow-up beyond five years is ongoing.

The objective of the COMMENCE trial is to confirm that the tissue processing, valve sterilization, and packaging for the Edwards pericardial aortic bioprosthesis model 11000A, do not raise new questions of safety and effectiveness in subjects who require replacement of their native or prosthetic aortic valve.

The trial population consists of adult subjects (18 years or older) diagnosed with aortic valve disease requiring a planned replacement of the native or prosthetic aortic valve. Concomitant coronary bypass surgery and ascending aorta resection and replacement from the sinotubular junction without the need for circulatory arrest are permitted.

Trial candidates with prior valve surgery which included the implant of a prosthetic valve or annuloplasty ring that will remain *in situ* are excluded. Concomitant valve repair or replacement are excluded. Surgical procedures outside the cardiac area are not permitted. Various clinical presentations and histories may cause exclusion from the trial.

The reporting period for the COMMENCE trial aortic arm is January 2013 through April 2021. At the time of the database lock, six hundred ninety-four (694) subjects were enrolled at twenty-seven (27) investigational sites in the US and Europe. Of the enrolled population, six hundred eighty-nine (689) subjects were successfully implanted with the model 11000A and left the operating room with the trial valve.

Table 2 provides trial demographics, NYHA Classification and Risk Scores; Table 3 lists the observed adverse event rates during study; Table 4 provides NYHA Classification data at baseline and 1 and 5-year follow-up; and Table 5 lists hemodynamic parameters at 1 and 5-years.

7.0 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 and as per guidelines (Refs. 10 and 11). Long-term anticoagulation and/or antiplatelet therapy should be considered for patients with risk factors for thromboembolism. Guidelines also recommend how to manage patients with bioprosthetic valve dysfunction and prophylaxis for infective endocarditis (Refs. 10 and 11).

7.1 Considerations in bioprosthetic valve selection

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. The ESC/EACTS (Ref. 10) and ACC/AHA (Ref. 11) Guidelines contain the complete recommendations for bioprosthetic valve selection.

Edwards encourages surgeons to participate in available registries when the INSPIRIS RESILIA aortic valve is implanted in younger patients.

7.2 Specific Patient Populations

The safety and effectiveness of the model 11500A valve 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 and adolescents;
- Patients with hypersensitivity to metal alloys that contain cobalt, chromium, nickel, molybdenum, manganese, carbon, beryllium and iron;
- Patients with hypersensitivity to latex;
- Patients with hypersensitivity to tissue with alpha-gal antigen.

8.0 Patient Counseling Information

Careful and continued medical follow up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed. Patients with valves 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 implant card at all times and to inform their healthcare providers that they have an implant when seeking care.

It is recommended that patients be briefed on warnings, precautions, contraindications, measures to be taken and limitations of use associated with the INSPIRIS RESILIA aortic valve, model 11500A.

9.0 How Supplied

9.1 Packaging

The INSPIRIS RESILIA aortic valve, model 11500A, is provided sterile and nonpyrogenic, in a double barrier tray package. The valve is sterilized by ethylene oxide. The net content of the package is one (1) valve. The double tray package is in a foil pouch which is in a carton. Upon receipt of the carton, inspect the exterior for signs of damage.

Each valve 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 valve, 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 valve and contact the local supplier or Edwards Lifesciences representative to make arrangements for return authorization and replacement.

WARNING: Carefully inspect the valve before implantation for evidence of extreme temperature exposure or other damage. Exposure of the valve to extreme temperatures will render the device unfit for use.

9.2 Storage

The INSPIRIS RESILIA aortic valve, model 11500A, should be stored at 10 °C to 25 °C (50 °F to 77 °F), in the foil pouch and shelf carton.

10.0 Directions for Use

10.1 Physician Training

The techniques for implanting this valve are similar to those used for any stented aortic surgical valve. No specific training or special facilities beyond that required for cardiac surgical procedures are required to implant the model 11500A.

The primary intended users are cardiac surgeons who perform these valve replacements and the staff (operating room nurses and technicians) responsible for preparation and implant of aortic or mitral valves.

10.2 Sizing

WARNING: Valve holders and fragments of handles and sizers are not radiopaque and cannot be located by means of an external imaging device. Loose fragments in the vasculature have the potential to embolize.

CAUTION: Do not use other manufacturer's valve sizers, or sizers for other Edwards Lifesciences valves, to size the INSPIRIS RESILIA aortic valve, model 11500A. Incorrect sizing may occur, which may result in valve damage, localized native tissue damage, and/or inadequate hemodynamic performance.

CAUTION: Examine sizers for signs of wear, such as dullness, cracking or crazing, prior to use. Replace sizer if any deterioration is observed. Continued use may result in fragmentation, embolization, or prolonged procedure.

10.2.1 Supra-annular sizing

Step	Procedure
1	For supra-annular implantation, the sewing ring of the valve is placed above the annulus, thereby maximizing the valve effective 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: a) Using the model 1133 sizer, select the cylindrical end of the largest diameter sizer that comfortably fits in the patient's annulus. b) 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 valve for implant. c) **Optional** - Determine if implanting a larger valve is possible by using the replica end of the next larger sizer. 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 the larger size replica end fits comfortably above the patient's annulus, implant this size of the valve. If the larger size replica end does not fit comfortably, implant the valve size identified in the previous step.

10.2.2 Intra-annular sizing

Step	Procedure
1	When an intra-annular technique is utilized, the entire valve including the sewing ring is placed inside the annulus. Either the cylindrical or replica end of the model 1133 sizer can be used for intra-annular sizing. For proper implantation of the valve in the intra-annular position, the sizer should be parallel with the plane of the annulus and the entire sizer, including the simulated sewing ring portion, should pass through the annulus.

10.3 Handling and Preparation Instructions

Step	Procedure
1	**WARNING: Check expiration date on packaging before use. Do not use product if expiration date has elapsed. This may result in compromised sterility.** **WARNING: Do not open foil pouch into sterile field. Foil pouch is a protective cover only. The outer surface of the outer tray is not sterile and may compromise the sterile field. The innermost package tray is sterile and may be introduced into the sterile field.** **CAUTION: Do not open the INSPIRIS RESILIA aortic valve, model 11500A package until implantation is certain.**
2	Once the appropriate size valve 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. Open pouch and remove tray in the non-sterile field (See Figure 7).
3	The valve inner tray is labeled with the work order number, model, size and serial number. The model, size and serial number should be confirmed with the number on the valve package and valve implant card. **CAUTION: If any difference in model, size or serial number is noted, the valve should not be implanted. If the incorrect size valve is used, valve damage, localized native tissue damage, and/or inadequate hemodynamic performance may result.**
4	Near the sterile field, hold the base of the outer tray and peel the lid from the outer tray.
5	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.
6	**CAUTION: Do not open the inner package until implantation is certain and the surgeon is ready to place the valve. Once the inner valve package is opened, the valve must be used immediately or discarded to minimize contamination and tissue dehydration.** **CAUTION: The valve is not secured to the inner tray. Care should be taken while peeling the lid and opening the plastic tab to prevent the valve from dislodging from the tray. Contamination, damage to the valve, and loss of sterility may result.** 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.
7	Attach the handle, model 1111 or model 1126, to the valve holder while the valve is still in the tray. To attach, insert the handle into the holder by aligning the handle with the threaded hole in the holder and turning the

Step	Procedure
	handle clockwise until a positive resistance is felt (See Figure 8). **CAUTION: Do not grasp the valve with hands or surgical instruments as damage to the valve may occur.** **CAUTION: Examine the handle for signs of wear, such as dullness, cracking or crazing, prior to use. Replace handle if any deterioration is observed. Continued use may result in fragmentation, embolization, or prolonged procedure.** **CAUTION: Do not push the valve off the aortic retainer while attaching the handle to the holder as this may result in the valve falling off the retainer. Contamination, damage to the valve, and loss of sterility may result.** **CAUTION: The handle/holder assembly is required for implantation and should not be removed until the valve is sutured to the annulus. This may result in improper seating of the valve.**
8	Once the handle is attached, remove the valve and aortic retainer from the inner tray.
9	To remove the aortic retainer from the valve, firmly grasp the aortic retainer from the finger slots and pull away from the handle/holder assembly (See Figure 9 and Figure 10).
10	**The model 11500A, DOES NOT REQUIRE RINSING prior to implantation.** **CAUTION: If the valve 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, as tissue dehydration can lead to valve dysfunction.** **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 INSPIRIS RESILIA aortic valve, model 11500A, is designed for supra-annular implantation and intra-annular implantation.

Step	Procedure
1	The surgeon should be familiar with the recommendations for proper sizing and placement in the supra-annular and/or intra-annular position (Refer to **Section 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: a) Surgically remove the diseased or damaged valve leaflets and all associated structures deemed necessary. b) Surgically remove any calcium from the annulus to ensure proper seating of the sewing ring of the valve to avoid damage to the delicate leaflet tissue. c) Measure the annulus using only the aortic sizers, model 1133. **CAUTION: When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the valve must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all the risks and benefits to the patient.**
2	**Supra-annular placement** A suture technique resulting in supra-annular placement of the valve, such as a non-everting horizontal mattress technique, should be employed. **Intra-annular placement** A suture technique resulting in intra-annular placement of the valve, such as an everting mattress technique, should be employed. Due to the relative flexibility of the frame, care must be exercised to prevent folding or deformation of the stent that may lead to regurgitation, altered hemodynamics, and/or leaflet disruption rendering the valve incompetent. In this regard, oversizing must be avoided.

Step	Procedure
3	The spacing of the sutures in the remnant of the valvular orifice and the valve sewing ring must be carefully matched to avoid folding of the leaflets or distortion of the orifice. Edwards Lifesciences has received reports in which individual mattress sutures, spanning a distance of 10 to 15 mm, produced a purse string effect causing compression of the valve orifice. 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. **CAUTION: Avoid placement of annular sutures deep into the adjacent tissue to avoid arrhythmias and conduction abnormalities.** **CAUTION: Avoid cutting or damaging the stent or delicate leaflet tissue when placing and cutting the sutures. This may result in valve dysfunction.** Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue. 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 valve. As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised to avoid looping or catching a suture around the commissure, which would interfere with proper valvular function. The stent of the aortic valve is symmetrical, and the commissure supports (struts) are equally spaced. The struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia.
4	The integral holder and attached handle are removed as a unit at the completion of the suturing procedure (see Figure 11). a) Using a scalpel, cut each of the three exposed sutures that are on the top of the holder. **CAUTION: Avoid cutting or damaging the stent or delicate leaflet tissue when cutting the holder sutures. This may result in valve dysfunction.** b) After all three holder sutures are cut, remove the handle/holder assembly, along with the holder sutures, from the valve as a unit. c) Remove the handle from the holder and discard the holder.

10.5 Accessory Cleaning and Sterilization

The accessories for the INSPIRIS RESILIA aortic valve, model 11500A, are packaged separately. The model 1126 handle is provided sterile and is intended for single use only. The model 1111 handle, the model 1133 sizers, and model TRAY1133 are reusable and are supplied nonsterile. Refer to the Instructions for Use supplied with the reusable accessories for cleaning and sterilization instructions.

10.6 Return of Valves

Edwards Lifesciences is interested in obtaining recovered clinical specimens of the INSPIRIS RESILIA aortic valve, model 11500A, for analysis. Contact the local representative for return of recovered valves.

- Unopened Package with Sterile Barrier Intact: If the foil pouch or trays have not been opened, return the valve in its original packaging.
- Package Opened but Valve is Not Implanted: If the tray is opened, the valve is no longer sterile. If the valve 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 Valve: The explanted valve 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.

10.7 Device Disposal

Used devices may be handled and disposed of in the same manner as hospital waste and biohazardous materials. There are no special risks related to the disposal of these devices.

11.0 MRI Safety Information

MR Conditional

Non-clinical testing has demonstrated that the INSPIRIS RESILIA aortic valve, model 11500A, is MR Conditional. A patient with the INSPIRIS RESILIA aortic valve, model 11500A, can be scanned safely under the following conditions:

- Static magnetic field of 1.5 tesla or 3 tesla only.
- Maximum spatial gradient magnetic field of 3,000 gauss/cm (30 T/m) or less.
- Maximum MR system-reported, whole-body averaged specific absorption rate (SAR) of 2.0 W/kg in Normal Operating Mode.

Under the scan conditions defined above, the INSPIRIS RESILIA aortic valve, model 11500A, is expected to produce a maximum *in vivo* temperature rise of less than 2.0 °C at 1.5 T and less than 2.5 °C at 3 T after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact extends approximately 10 mm from the model 11500A valve when imaged with a spin echo pulse sequence and 17 mm from the device when imaged with a gradient echo pulse sequence and a 3 tesla MRI system. The artifact obscures the device lumen.

12.0 Qualitative and Quantitative Information

This device contains or incorporates tissues or cells of animal origin. The valve leaflets are made of bovine pericardial tissue.

This device contains the following substance(s) defined as CMR 1B in a concentration above 0.1% weight by weight:

Cobalt; CAS No. 7440-48-4; EC No. 231-158-0

Current scientific evidence supports that medical devices manufactured from cobalt alloys or stainless steel alloys containing cobalt do not cause an increased risk of cancer or adverse reproductive effects.

The following table shows the qualitative and quantitative information on the materials and substances:

Substance	CAS	Model Mass Range (mg)
Polytetrafluoroethylene	9002-84-0	484 - 808
Glycerol	56-81-5	231 - 533
Cobalt	7440-48-4	110 - 271
Polyethylene terephthalate	25038-59-9	101 - 169
Chromium	7440-47-3	53.5 - 139
Collagens, bovine, polymers with glutaraldehyde	2370819-60-4	62.5 - 129
Iron	7439-89-6	28.5 - 125
Nickel	7440-02-0	40.8 - 106
Polydimethylsiloxane	63148-62-9	40.6 - 77.8
Molybdenum	7439-98-7	19.0 - 49.5
Silicon dioxide	7631-86-9	16.6 - 32.8
Manganese	7439-96-5	4.93 - 14.9
Silicon	7440-21-3	0 - 6.61
Fibroin Silk	9007-76-5	1.72 - 3.17
Barium sulfate	7727-43-7	1.18 - 2.23
Carbon	7440-44-0	0 - 0.661
Titanium dioxide	13463-67-7	0.149 - 0.500
Polyethylene terephthalate-isophthalate copolymer	24938-04-3	0.211 - 0.466
Antimony trioxide	1309-64-4	0.0835 - 0.193
Octamethylcyclotetrasiloxane; D4	556-67-2	0.0625 - 0.118
Beeswax	8012-89-3	0.0554 - 0.118
Carbon black	1333-86-4	0.0393 - 0.0661
Phosphorus	7723-14-0	0 - 0.0661
Sulfur	7704-34-9	0 - 0.0661
Decamethylcyclopentasiloxane; D5	541-02-6	0.0165 - 0.0313
Logwood Extract Dye	475-25-2	0.0139 - 0.0254
Dodecamethylcyclohexasiloxane; D6	540-97-6	0.0112 - 0.0212
Beryllium	7440-41-7	0 - 0.00661
Erucamide	112-84-5	0.00268 - 0.00544
2,5-Bis(5-tert-butyl-2-benzoxazolyl)thiophene	7128-64-5	0.000285 - 0.000680
4-Dodecylbenzenesulfonic acid	121-65-3	0.0000854 - 0.000140

13.0 Summary of Safety and Clinical Performance (SSCP)

Refer to https://meddeviceinfo.edwards.com/ for a SSCP for this medical device.

After the launch of the European Database on Medical Devices/ Eudamed, refer to https://ec.europa.eu/tools/eudamed for a SSCP for this medical device.

14.0 Patient Labeling

A patient implant card is provided with each valve. After implantation, please complete all requested information and provide the implant card to the patient. The serial number is found on the package. This implant card allows patients to inform healthcare providers what type of implant they have when they seek care.

15.0 Basic Unique Device Identification-Device Identifier (UDI-DI)

The Basic UDI-DI is the access key for device-related information entered in the Eudamed.

The following table contains the Basic UDI-DI:

Product	INSPIRIS RESILIA Aortic Valve
Model	11500A
Basic UDI-DI	0690103D002IRV000Y9

16.0 Expected Lifetime of the Device

The claimed lifetime of the INSPIRIS RESILIA aortic valve is 5 years.

The INSPIRIS RESILIA aortic valve has been subjected to rigorous pre-clinical durability and fatigue reliability testing in accordance with internationally recognized valve testing standards to 5 years. In addition, durability is supported by 5 years of clinical follow-up in the COMMENCE trial; refer to **Section 6. 0 Clinical Studies**. Actual lifetime performance depends on multiple biological factors and can vary from patient to patient.

17.0 References

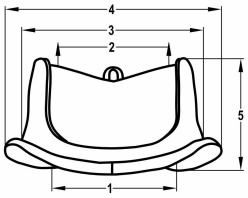
1. Flameng et. al. A randomized assessment of an advanced tissue preservation technology in the juvenile sheep model. *J. Thorac Cardiovasc Surg*, Article in Press, 2014. [Valves with Edwards XenoLogiX™ treatment were used as controls.]
2. Rabbit Calcification Study on Edwards and Competitor Tissue Heart Valves. Study on file at Edwards.
3. Reis, Robert L., et al. The Flexible Stent. A new concept in the fabrication of tissue heart valve prostheses. *J. Thorac Cardiovasc Surg* 1971, 62(5):683:689.
4. Barrat-Boyes, B.G. and A.H.G. Roche. A review of aortic valve homografts over a six and one-half year period. *Ann Surg* 1969, 170:483-492.
5. Brewer, R.J., et al. The dynamic aortic root. Its role in aortic valve function. *J Thorac Cardiovasc Surg* 1976, 72:413-417.
6. Dvir et al. Transcatheter Aortic Valve Implantation in Failed Bioprosthetic Surgical Valves, *JAMA* 2014
7. Dvir et al. Transcatheter Aortic Valve Replacement for Degenerative Bioprosthetic Surgical Valves: Results from the Global Valve-in-Valve Registry, *Circulation* 2012
8. Candice Baldeo et al. Does chemo-radiation predispose to structural valve deterioration? *International Journal of Cardiology* 211 (2016) 53-54
9. Syed Wamique Yusuf, et al., Radiation-induced heart disease: a clinical update, *Cardiol. Res. Pract.* (2011), 317659 9 pages
10. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* Feb 12 2022; 43(7):561-632. doi:10.1093/eurheartj/ehab395
11. Writing Committee M, Otto CM, Nishimura RA, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Thorac Cardiovasc Surg.* Aug 2021;162(2):e183-e353. doi:10.1016/j.jtcvs.2021.04.002

For a patient/user/third party in the European Economic area; if, during the use of this device or as a result of its use, a serious incident has occurred, please report it to the manufacturer and your national competent authority, which can be found at http://ec.europa.eu/growth/sectors/medical-devices/contacts_en.

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

Table 1: Nominal Dimensions

INSPIRIS RESILIA Aortic Valve, Model 11500A



Size	19 mm	21 mm	23 mm	25 mm	27 mm	29 mm
1. Inflow Orifice Diameter (mm)	17.0	19.0	21.0	23.0	25.0	27.0
2. Effective Orifice Diameter (mm)	15.5	18.0	17.5	19.0	21.0	24.0
3. Valve Housing External Diameter (mm)	19.0	21.0	23.0	25.0	27.0	29.0
4. External Sewing Ring Diameter (mm)	24.0	26.5	29.0	31.0	33.0	35.0
5. Total Profile Height (mm)	13	14	15	16	17	18

Note: For Sizing, Refer to Section 10.4 Device Implantation

Table 2: COMMENCE Trial Study Demographics

Age at Implant	N: Mean ± SD (Min, Max)
Age (years)	694: 67.0 ± 11.6 (20.0, 90.0)
Sex	**% (n/N)**
Female	28.2% (196/694)
Male	71.8% (498/694)

Age at Implant	N: Mean ± SD (Min, Max)
NYHA Classification	**% (n/N)**
Class I	23.6% (164/694)
Class II	50.0% (347/694)
Class III	24.5% (170/694)
Class IV	1.9% (13/694)
Risk Scores	**N: Mean ± SD (Min, Max)**
STS risk of mortality (%)[1]	539: 2.0 ± 1.8 (0.3, 17.5)
EuroSCORE II (%)	694: 2.6 ± 3.0 (0.5, 24.6)

N is the number of subjects with available data for the given parameter.

[1] STS scores only calculated for subjects undergoing isolated AVR or AVR+CABG.

Table 3: Observed Adverse Events

Adverse Event or Outcome	Early[1] (N = 694) n, m (%)	Late[2] (LPY[3] = 3144.94) n, m (%/pt-yr)	Freedom-from Event at 5 Years (SE)[4]
All mortality	9, 9 (1.3%)	71, 71 (2.3%)	89.26 (1.24)
Valve-related mortality	3, 3 (0.4)	18, 18 (0.6%)	96.90 (0.70)
Reoperation	1, 1 (0.1%)	11, 11 (0.3%)	98.72 (0.45)
Explant	0, 0 (0.0%)	8, 8 (0.3%)	99.03 (0.40)
Thromboembolism	16, 16 (2.3%)	45, 52 (1.7%)	91.08 (1.13)
Valve thrombosis	0, 0 (0.0)	1, 1 (0.0%)	100.00 (0.000)
Endocarditis	0, 0 (0.0)	13, 14 (0.4%)	97.84 (0.60)
All bleeding	7, 7 (1.0%)	67, 82 (2.6%)	89.26 (1.25)
Major bleed	5, 5 (0.7%)	34, 42 (1.3%)	94.38 (0.93)
All Paravalvular Leak	2, 2 (0.3)	3, 3 (0.1%)	99.23 (0.34)
Major PVL	1, 1 (0.1%)	2, 2 (0.1%)	99.54 (0.26)
Structural Valve Deterioration	0, 0 (0.0)	3, 3 (0.1%)	100.00 (0.000)

[1] For 'Early Events' (events occurring thru post-implant day 30): For 'Early' m is the number of events; n is the number of subjects experiencing an event; % = n/N.

[2] For 'Late Events' (events occurring after post-implant day 30): m is the number of events; n is the number of subjects experiencing an event; and % = m/LPY.

[3] LPY: Late patient-years; LPY are calculated from post-implant day 31 until the last patient contact.

[4] Based on Kaplan-Meier analysis of time to first occurrence (early or late). Standard Error (SE) based on Greenwood's formula.

Table 4: NYHA Classification at Baseline, 1 and 5 Years

NYHA Class	Baseline NYHA % (n/N[1])	1-Year NYHA % (n/N[1])	5-Year NYHA % (n/N[1])
Class I	23.8% (164/689)	81.8% (523/639)	75.9% (368/485)
Class II	49.9% (344/689)	16.4% (105/639)	21.4% (104/485)
Class III	24.4% (168/689)	1.4% (9/639)	2.1% (10/485)
Class IV	1.9% (13/689)	0.3% (2/639)	0.6% (3/485)

[1] N is the number of subjects with known NYHA at the specified post-operative visit.

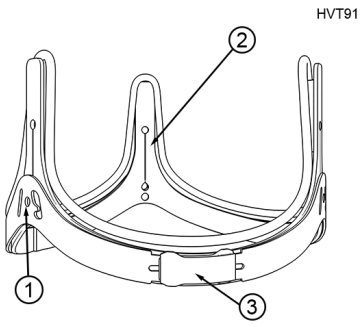
Table 5: Hemodynamic Parameters at 1 and 5 Years

Visit	19 mm N: Mean ± SD	21 mm N: Mean ± SD	23 mm N: Mean ± SD	25 mm N: Mean ± SD	27 mm N: Mean ± SD	29 mm N: Mean ± SD
EOA (cm^2)						
1 Year	20: 1.06 ± 0.19	121: 1.33 ± 0.35	188: 1.56 ± 0.42	184: 1.79 ± 0.44	92: 2.24 ± 0.58	18: 2.39 ± 0 .53
5 Years	16: 1.02 ± 0.28	79: 1.19 ± 0.31	121: 1.42 ± 0.38	128: 1.69 ± 0.49	74: 2.09 ± 0.59	9: 2.21 ± 0.49
Mean Gradient (mmHg)						

Visit	19 mm N: Mean ± SD	21 mm N: Mean ± SD	23 mm N: Mean ± SD	25 mm N: Mean ± SD	27 mm N: Mean ± SD	29 mm N: Mean ± SD
1 Year	20: 18.73 ± 9.06	122: 12.59 ± 4.82	193: 10.37 ± 3.78	185: 9.11 ± 3.35	93: 8.07 ± 3.30	18: 6.19 ± 2.06
5 Years	16: 21.45 ± 12.98	80: 14.08 ± 6.37	122: 12.03 ± 5.12	128: 10.32 ± 4.26	74: 8.75 ± 4.08	9: 7.86 ± 2.01

N represents the number of subjects with evaluable data.

Figures



1. Size Markers
2. Perforated Polyester Support Band
3. Expansion Zone

Figure 1

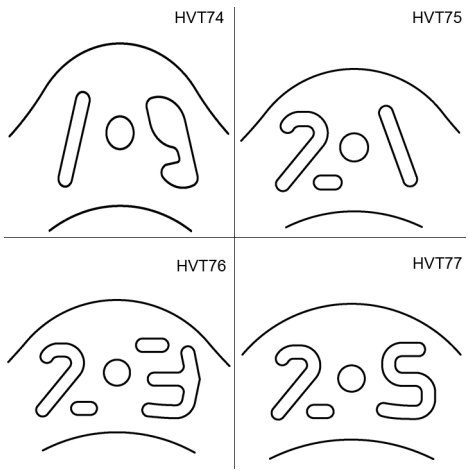
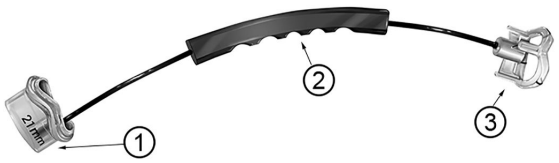


Figure 2

Figure 3: Model 11500A (sizes 19 – 25 mm)

Figure 4: Model 11500A (sizes 27 and 29 mm)

Figure 5: Model 3300TFX (sizes 19 – 29 mm)



1. Cylindrical end
2. Handle
3. Replica end

Figure 6

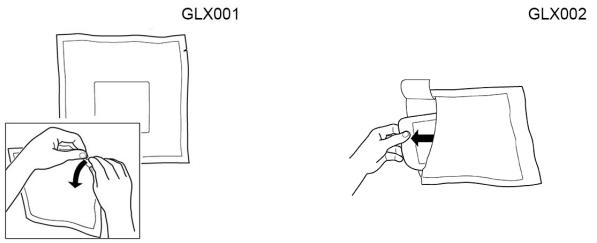


Figure 7

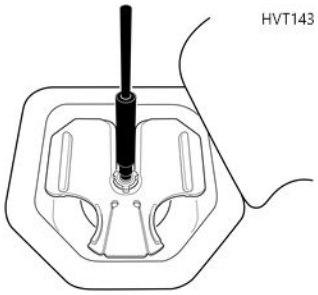


Figure 8

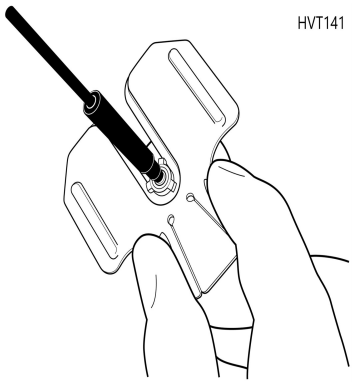


Figure 9

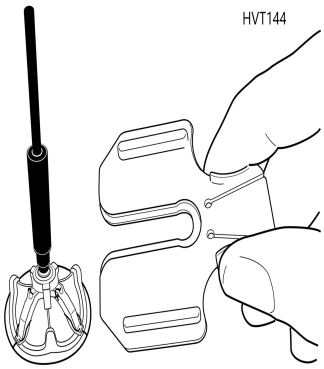


Figure 10

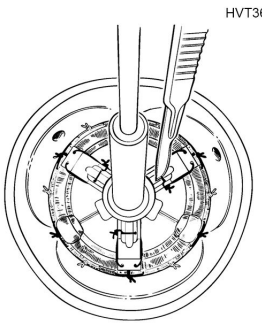
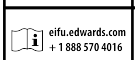


Figure 11

Symbol Legend

	English
	Model Number
	Do not re-use
	Caution
	Consult instructions for use
	Consult instructions for use on the website
	Do not use if package is damaged and consult instructions for use
	Temperature limit
	Sterilized using ethylene oxide
	Use product if indication is shown

	English
	Double sterile barrier system
	Quantity
	Use-by date
	Serial Number
	Unique Device Identifier
	Size
	Manufacturer
	Date of manufacture

	English
	Authorized representative in the European Community/European Union
	Do not use product if indication is shown
	MR Conditional
	Non-pyrogenic
	Medical device
	Contains biological material of animal origin
	Contains hazardous substances
	Importer
	Work Order

EC REP

Edwards Lifesciences GmbH
Parkring 30
85748 Garching bei München
Germany

CE 0344

2024-05
10050982001 A

Edwards Lifesciences LLC
One Edwards Way
Irvine, CA 92614 USA

Edwards Lifesciences B.V.
Verlengde Poolseweg 16
4818 CL Breda, Netherlands

Telephone +1.949.250.2500
+1.800.424.3278
FAX +1.949.250.2525

Web IFU