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**FORMAL REQUEST FOR A MEDICARE NATIONAL COVERAGE DETERMINATION (NCD)
Transcatheter Aortic Valve Replacement (TAVR) Procedures**

Dear Dr. Jacques:

The Society of Thoracic Surgeons (STS) and the American College of Cardiology (ACC) are submitting a formal request that the Centers for Medicare and Medicaid Services (CMS) develop a National Coverage Determination (NCD) for transcatheter aortic valve replacement (TAVR) procedures. This letter follows a previous, informal application sent on July 8, 2011.

TAVR is a procedure that allows deployment of a bioprosthetic aortic valve currently utilizing one of two minimally invasive techniques: either transfemoral or transapical. There are a number of transcatheter devices for aortic valve implantation procedures that are in development; however none of these devices have received Food and Drug Administration (FDA) approval. The Edwards Life Sciences Sapien TAVR device is expected to be the first to receive FDA approval.

The cardiology and cardiac surgery specialty societies ACC and STS formally request an NCD to ensure that TAVR technology is used in a manner that is most beneficial to Medicare patients. A recent clinical trial that focused on the use of TAVR to treat aortic stenosis in high-risk operative and/or inoperable candidates demonstrated that TAVR was a superior alternative to medical management in inoperable patients and “non-inferior” in patients at high risk for open heart surgery. The clinical trial demonstrated that the most successful patient outcomes occur when the following criteria are met: the procedure is performed in a specialized heart center and managed using a multidisciplinary team in which each member has appropriate training and credentialing (for which requirements are currently under development), the procedure is performed in a modified conventional cardiac laboratory or hybrid operating room that contains the specialized equipment necessary for the procedure, and the multidisciplinary team uses a planned approach to co-management decision making as well as technical insertion of the device.

In addition, the specialty societies feel that it is critical that long-term outcome analysis and on-going analysis of data are performed by continuous review of the data and refinement of recommendations. In order to accomplish this, the specialty societies are recommending that CMS include as a condition of coverage mandatory reporting of the procedures in an STS-ACC

Transcatheter Valvular Therapy (TVT) Registry which would include long term follow-up using CMS data.

The specialty societies feel that CMS is best equipped to ensure the appropriate utilization of TAVR technology by developing an NCD that ensures that the procedure is:

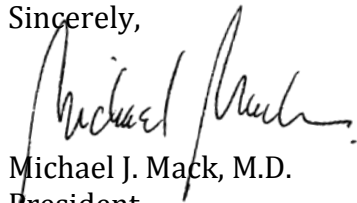
- Performed in a specialized heart center utilizing a modified conventional cardiac laboratory or hybrid operating room that contains the specialized equipment necessary for the procedure;
- Managed using a multidisciplinary team using planned approach to co-management decision making as well as technical insertion of the device;
- Reported on using a joint STS-ACC TVT Registry.

We believe that all of these factors can be best addressed successfully through an NCD, thereby ensuring safe, effective, and appropriate use of this new technology for Medicare beneficiaries.

We have included the following supplemental information to support this formal request:

Coverage Language Summary
TAVR Research Bibliography
TVTR Summary
Credentialing Document Summary

Sincerely,



Michael J. Mack, M.D.
President
The Society of Thoracic Surgeons



David R. Holmes, Jr., M.D., F.A.C.C.
President
American College of Cardiology

The American College of Cardiology Foundation (ACCF) and The Society of Thoracic Surgeons (STS) have large, mature, extensive national registries used by over 90% of cardiac centers in the country. The data are formally audited by independent, on-site reviews to ensure accurate data quality. Database managers are well-trained through a variety of measures including conference calls, one-on-one instruction, and a national conference specifically focused on data entry.

These registries provide in-depth clinical information including risk-adjusted outcomes for a variety of procedures. The short-term outcomes from these clinical registries can be linked to long-term outcomes and cost information from CMS data. This type of registry, made up of "real-world" patients, provides the ideal substrate for device surveillance, appropriateness of care analysis, and comparative effectiveness research (CER).

Device evaluation typically is based on the highly selective patient populations studied in early clinical trials. With new treatment options becoming available in the field of valvular heart disease, the need for a national registry becomes compelling. CER will provide information to determine appropriateness of care and device surveillance will monitor the safety and effectiveness of new technologic advances.

The present approach relies upon industry-developed registries. This is a major expense to industry and creates potential for conflict of interest. In addition, the process is wasteful and inefficient by creating registries for each device when, in fact, one registry for many devices would avoid duplication and conflicting standards.

The STS and ACCF can develop a single, generic registry of this type. The initial registry will be designed to capture data on all patients receiving transcatheter aortic valve replacement (TAVR) in this country, and will also serve as the platform for future aortic and other valve device post market surveillance. Immediate comparison with surgical aortic valve replacement (AVR) will be possible by linkage to the existing STS database. Future efforts may include patients in a more global area such as medical treatment of aortic stenosis via linkage with the National Cardiovascular Data Registry PINNACLE Registry (outpatient) thereby creating a truly disease based registry.

The STS-ACC TVT (Transcatheter Valvular Therapy) Registry will be designed to monitor device iterations as well as devices from a variety of manufacturers, with the first application of the registry serving as device surveillance and outcomes evaluation of the Edwards Lifesciences SAPIEN transcatheter valve.

Definitions of the parameters to be collected will be harmonized to be consistent with definitions from the Valve Academic Research Consortium (VARC). The analyses will be performed by the Duke Clinical Research Institute (DCRI) and will include long-term follow-up with linked CMS MedPAR data. Reports can be tailored to meet the expectations of government agencies as well as those of industry and the national professional societies.

This operational model will streamline the process of device evaluation and will facilitate defining appropriateness of care, thereby minimizing the risk of overuse. The TVT Registry should serve as a prototype for registry-based analyses across the entire field of medicine.

Credentialing Document Summary

A multisociety, multidisciplinary writing committee including the American Association for Thoracic Surgery, American College of Cardiology, the Society for Cardiovascular Angiography and Intervention, and The Society of Thoracic Surgeons is currently developing a position paper to address operator and institutional requirements for transcatheter valve repair and replacement. The document will address operator training and credentialing, institutional requirements, patient selection and management, and procedure performance.

The timeline for this document is quite aggressive with an expected completion of the first draft **by September 30, 2011.**

Benefit Category

Physician Services

Inpatient Hospital Services

Note: This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

Item/Service Description

A. General

The TAVR procedure involves the insertion of a bioprosthetic aortic valve at the site of the native aortic valve. It is deployed using catheter based technology. The aortic valve can be deployed using: 1) a percutaneous transarterial approach through a peripheral artery 2) a transaortic approach through a limited sternotomy or 3) a transapical approach with a transthoracic technique (limited lower thoracotomy). Any of these approaches may or may not require cardiopulmonary bypass. The decision on transarterial or transapical catheter access to the aortic valve depends on the size of the peripheral and central arteries and the degree and severity of atherosclerotic involvement of the aorto iliac tree and aorta.

Indications and Limitations of Coverage

B. Nationally Covered Indications

TAVR is covered when performed in the following patient populations and additional patient populations in accordance with future FDA-approved labeling:

Patient populations

A. High Risk Surgical Candidates:

In order to qualify as a high-risk surgical candidate, the patient must meet all of the following criteria:

- Patients must have co-morbidities such that the surgeon and cardiologist concur that the predicted risk of operative mortality is 15% and the patient has a minimum Society of Thoracic Surgeons (STS) risk score of 8 or significant co-morbidities including but not limited to heavily calcified (porcelain) aorta, previous chest radiation therapy, advanced liver disease, advanced frailty.
- The surgeon's assessment of operative co-morbidities not captured by the STS score must be documented in the patient medical record.
- Patient has severe degenerative aortic valve stenosis as defined by ACC/AHA guidelines.
- Patient is symptomatic from his/her aortic valve stenosis, as demonstrated by NYHA Functional Class II or greater.

B. Inoperable Candidates:

In order to qualify as an inoperable candidate, the patient must meet all of the following criteria:

- Patient has severe degenerative aortic valve stenosis as defined by ACC/AHA guidelines.
- Patient is symptomatic from his/her aortic valve stenosis, as demonstrated by NYHA Functional Class II or greater.
- The patient and the multidisciplinary team, after formal consultations by a cardiologist and two cardiovascular surgeons, agree that medical factors preclude operation, based on a conclusion that the probability of death or serious, irreversible morbidity exceeds the probability of meaningful improvement. Specifically, the probability of death or serious, irreversible morbidity should exceed 50%. The surgeons' consult notes shall specify the medical or anatomic factors leading to that conclusion and include documentation of the STS score to additionally identify the risks in these patients.

TAVR is covered only when the following additional requirements are met:

1. National TVT Registry

- a. The patient, the treating cardiologist, and surgeon agree that the patient will be required to participate in a national transcatheter valve (TVT) clinical registry. This registry must enroll all consecutive patients undergoing TAVR at all institutions. It will include clinical and administrative data for early and longer term follow up of patients. The data will be adjudicated. It will include detailed information about patient selection criteria, procedural performance, complications and long term analysis of hard end points such as death, stroke and infarction and device performance and softer endpoints. The registry must allow the tracking of changes in patient selection criteria, and outcomes with new device iterations, or new devices from different manufacturers. A specific data analytic center must be identified to manage the detailed case report forms. Such a registry will need a dedicated steering committee which includes trial design individuals, surgeons and interventional cardiologists.

2. Facility requirements

- a. TAVR is reasonable and necessary when performed at facilities that are identified as regional centers for structural heart valve disease. To qualify as a regional center, a hospital must have one of the procedural settings and/or specialized equipment for the TAVR outlined below in addition to minimal volume requirements for the treatment of aortic valve disease as defined by the specialty societies' consensus document:
- b. Modified/ Hybrid Catheterization Laboratory
 - i. Laboratory should be large enough to hold the recommended equipment,
 - ii. Anesthesia equipment,
 - iii. Transesophageal echocardiography machines,
 - iv. 3-dimensional intravascular ultrasound images,
 - v. Intraaortic balloon pumps,

- vi. Cardiopulmonary bypass machines,
 - vii. Surgical sterility standards including airflow exchanges.
- c. Hybrid Operating Room
- i. Operating room should be large enough to hold the recommended equipment,
 - ii. Catheterization laboratory– quality X-ray imaging,
 - iii. Transesophageal echocardiography,
 - iv. 3-dimensional intravascular ultrasound images,
 - v. Intraaortic balloon pumps,
 - vi. Cardiopulmonary bypass machines, and
 - vii. Rotational angiography.
3. Multi-disciplinary team and provider requirements
- a. Coverage is limited to providers who are part of a multidisciplinary team that will be central in applying the STS standardized scoring system to evaluate risk-benefit profiles in this diverse group of patients. This scoring system along with joint cardiology and cardiac surgeon clinical judgment will be used to reach a final decision regarding the appropriate use of TAVR. The patient’s values and goals need to be central in benefit-risk assessment and treatment decisions. The team may include individuals representing the following specialties:
 - i. Primary cardiologists
 - ii. Cardiac surgeons
 - iii. Interventional cardiologists
 - iv. Echocardiographers and imaging specialists
 - v. Heart failure specialists
 - vi. Cardiac anesthesiologists
 - b. Coverage is limited to facilities/providers where both the cardiologist and cardiac surgeon participate jointly in the intra-operative technical aspects of TAVR (the “team approach”).
 - c. Coverage is limited to cardiologists and cardiac surgeons who have been properly trained and credentialed in the procedure. Credentialing requirements will be in accordance with the specialty societies’ consensus document. Providers of this service must also document that all ancillary personnel, including physicians, nurses, operating room personnel and technicians, are trained in the procedure and the proper use of the equipment involved.
 - d. Coverage is limited to cardiologists and cardiac surgeons who participate in the national TVT Registry.

C. Nationally Non-Covered Indications

- 1. TAVR is not covered in any of the following clinical circumstances:**

- a. Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation >3+).
- b. Isolated aortic regurgitation
- c. Untreated clinically significant coronary artery disease requiring revascularization.
- d. Hypertrophic cardiomyopathy with or without obstruction (HOCM).
- e. Echocardiographic evidence of intracardiac mass, thrombus or vegetation.
- f. Life expectancy < 12 months due to non-cardiac co-morbid conditions.
- g. Significant aortic disease, including untreated abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5cm or greater; marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe “unfolding” and tortuosity of the thoracic aorta unless the patient qualifies for a transapical or other aortic or subclavian approaches.
- h. Iliofemoral vessel characteristics that would preclude safe placement of an introducer sheath such as severe obstructive calcification, severe tortuosity or vessels size in patients who are considered candidates for a trans-femoral approach unless the patient qualifies for a transapical or other aortic approach.

2. All other indications for the use of TAVR not otherwise listed remain non-covered, except in the context of Category B investigational device exemption clinical trials (42 CFR 405) or as a routine cost in clinical trials defined under section 310.1 of the NCD Manual.

D. National Coverage with Evidence Development

TAVR is only covered under CED in the following clinical circumstances:

- Aortic valve is a congenital unicuspid or bicuspid valve; or is non-calcified.
- Pre-existing prosthetic heart valve in any position, prosthetic ring, or severe (greater than 3+) mitral insufficiency.
- Severe ventricular dysfunction with LVEF < 20 .
- Renal insufficiency (Creatinine > 3.0) and/or end stage renal disease requiring chronic dialysis.
- Low gradient low output aortic stenosis.
- Patients who have significant associated valvular lesions which cannot be treated surgically.

TAVR will be covered by Medicare when studied in a prospective clinical trial that addresses one or more of the following questions:

- In Medicare aged patients does TAVR affect outcomes with respect to:
 - Mortality
 - Functional improvement per NYHA functional class
 - Stroke
 - Other major adverse cardiovascular events
 - Length of hospital stay

- Valve function
- Quality of life.

Potential patient populations that may be studied in future clinical trials include:

- a. Patients with a STS Risk score between 4 and 8,
- b. “Valve in Valve” therapy, and
- c. ESRD.

The clinical study must adhere to the standards of scientific integrity and relevance to the Medicare population. (See Attachment I)

Attachment I

- a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
- b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
- c. The research study does not unjustifiably duplicate existing studies.
- d. The research study design is appropriate to answer the research question being asked in the study.
- e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
- f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the FDA, it must be in compliance with 21 CFR Parts 50 and 56.
- g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see <http://www.icmje.org>).
- h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for CED coverage.
- i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.
- j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.
- k. The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured, including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (<http://www.icmje.org>). However, a full report of the outcomes must be made public no later than three (3) years after the end of data collection.
- l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
- m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability, or Medicaid eligibility.

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**Supplemental Information for a Request for a
Medicare National Coverage Determination (NCD)
Transcatheter Valve Replacement Procedures
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1. Benefit categories

Physician services
Inpatient hospital services

2. Description of the Transcatheter Aortic Valve Replacement (TAVR)

TAVR represents an emerging technology to treat high-risk and elderly symptomatic patients with severe aortic stenosis. Candidates for this technology are either non-operative candidates or high-risk operative candidates as determined using the STS risk score and other clinical criteria.

The TAVR procedure involves the insertion of a bioprosthetic aortic valve at the site of the native aortic valve. It is deployed using catheter based technology. The aortic valve can be deployed using: 1) a percutaneous transarterial approach through a peripheral artery 2) a transaortic approach through a limited sternotomy or 3) a transapical approach with a transthoracic technique (limited lower thoracotomy). Any of these approaches may or may not require cardiopulmonary bypass. The decision on transarterial or transapical catheter access to the aortic valve depends on the size of the peripheral and central arteries and the degree and severity of atherosclerotic involvement of the aorto iliac tree and aorta.

Detailed description of the procedure

Percutaneous transarterial aortic valve replacement

If general anesthesia is used, the patient is intubated and connected to a mechanical ventilator. The patient is prepped and draped. Heparin anticoagulation is administered when indicated. Pulmonary and radial artery catheters are routinely inserted for hemodynamic monitoring. The heart rate and rhythm are monitored throughout the procedure. Transesophageal echocardiography (TEE) is also used routinely by an experienced echocardiographer and/or echo certified anesthesiologist to confirm aortic valve annular diameter and proper valve placement as well as assessment of post procedure paravalvular leaks (if performed, TEE is separately reported). A temporary transvenous pacemaker electrode is advanced into apex of the right ventricle and tested for proper electrical capture.

Femoral, radial or brachial arterial access for the reference pigtail catheter is obtained by needle puncture (Seldinger technique), followed by passage of a standard guidewire and pigtail angiographic catheter. The catheter is positioned within the aortic root using fluoroscopy. A root aortogram(s) is/are obtained using power contrast injection and cine angiography to determine the optimal angiographic angle relative to the native aortic valve.

Arterial access (most commonly femoral, but may be axillary or subclavian) for the delivery catheter is obtained via needle puncture or direct surgical exposure (when open arterial access is performed, it is separately reported). After contrast injection, angiography of the access vessel is performed to confirm anatomical suitability of the vessel for passage of the delivery catheter. Using fluoroscopic guidance, a standard guidewire is advanced to the descending aorta and exchanged for a stiff guidewire with an angiographic catheter. Over the stiff guidewire, a large-bore vessel introducer sheath is inserted and advanced to a level that is inferior to the renal arteries. The guidewire is removed and anticoagulation therapy is administered to achieve therapeutic anticoagulation levels.

Under fluoroscopic guidance, guidewire access across the native aortic valve is obtained using a guidewire and catheter. The guidewire is exchanged for a stiff guidewire and a balloon aortic valvuloplasty catheter is passed over the guidewire and positioned within the native aortic valve. Balloon aortic valvuloplasty is performed during rapid burst ventricular pacing which is used to obtain optimal catheter position. Concurrently, a trained assistant, as directed by the physician, loads the prosthetic valve into or onto the delivery catheter. Note: correct orientation of the valve on the delivery catheter is confirmed by the physician, before inserting the valve-delivery catheter system into the introducer sheath. The valvuloplasty catheter is exchanged for the prosthetic delivery catheter over the previously-positioned stiff guidewire while maintaining access across the native aortic valve. The delivery catheter is advanced to the aortic root and positioned across the native aortic valve annulus under fluoroscopic guidance. In addition, transesophageal echocardiography may be used to position the prosthesis within the aortic annulus (if performed, TEE is separately reported). Multiple root aortograms may be performed to facilitate placement before a satisfactory valve position is chosen. Deployment of the prosthesis is performed usually with rapid burst ventricular pacing.

After confirming satisfactory position and function of the valve, as well as assessing the degree of any paravalvular regurgitation, the delivery catheter, guidewire, and sheath are removed from the patient. The arterial access site is closed via direct suture or closure with percutaneous closure devices. If heparin was administered, it is reversed using protamine. A sterile dressing is applied to the entry site.

Transapical aortic valve replacement

After general anesthesia is induced, the patient is intubated and connected to a mechanical ventilator and adequate exposure of the heart and control of the left ventricular apex is obtained (reported separately 334X1 or X2). The use of cardiopulmonary bypass is seldom (<5%) necessary but is available (see below). A soft J-wire is inserted through the cardiac apex across the aortic valve under fluoroscopy. After advancing a pigtail catheter over the J-wire, the wire is exchanged for a stiffer wire. This wire is advanced beyond the thoracic aorta. An aortic root angiogram is obtained to establish the precise location of the aortic valve. Multiple root aortograms may be required to achieve the proper image intensifier angle relative to the native aortic valve.

Under fluoroscopy, a balloon aortic valvuloplasty catheter is passed over the wire, and centered within the native aortic valve. Balloon valvuloplasty is performed during rapid ventricular pacing. Concurrently, a trained assistant, as directed by the physician, loads the prosthetic valve into or onto the delivery catheter. The balloon aortic valvuloplasty catheter is then exchanged for the larger, transapical sheath, which is advanced several centimeters into the left ventricular cavity. The orientation of the valve on the catheter is confirmed by the physician, before inserting the valve-catheter system through the transapical sheath. Under fluoroscopy, the valve is positioned within the aortic annulus. In addition, transesophageal echocardiography may be used to position the prosthesis within the aortic annulus (TEE is separately reported). Multiple root aortograms may facilitate placement before a satisfactory valve position is chosen. Deployment of the valve may be performed during rapid ventricular pacing.

After confirming satisfactory position and function of the valve, as well as assessing the degree of any paravalvular regurgitation, the catheter and guidewire are removed. Completion of the procedure is accomplished.

Transapical approach without cardiopulmonary bypass:

The heart is exposed through a small left anterior limited thoracotomy in the fifth or sixth intercostal space. A pericardiotomy is performed, and pacing wires are affixed to the ventricular muscle. Two circumferential pledgeted pursestring sutures are placed in the apex of the left ventricle. At the completion of the valve implant procedure (reported separately) the LV apical sheath is removed and the pursestring sutures are tied. Hemostasis is assured. Protamine is given to reverse the heparin. Chest tube(s) are placed. The incision is closed in layers and dressings are placed.

Transapical approach with cardiopulmonary bypass:

Heparin is administered. The right axillary artery is surgically exposed, a graft attached and end-to-side anastomosis, and cannulated for arterial inflow. A venous drainage catheter is placed percutaneously or through surgical exposure of the right femoral vein. It is positioned in the superior vena cava using fluoroscopic or echocardiographic guidance. Cardiopulmonary bypass is initiated at normothermia. The heart is exposed through a small left anterior limited thoracotomy in the fifth or sixth intercostal space. A pericardiotomy is performed, and pacing wires are affixed to the ventricular muscle. Two circumferential pledgeted pursestring sutures are placed in the apex of the left ventricle. At the completion of the valve implant procedure (reported separately) the LV apical sheath is removed and the pursestring sutures are tied. Hemostasis is assured. The patient is weaned from cardiopulmonary bypass and decannulated. Protamine is given to reverse the heparin. Chest tube(s) are placed. The incisions are closed in layers and dressings are placed.

3. The target Medicare population and medical conditions for which the TAVR can be used

The initial experience with TAVR for aortic stenosis has been positive with evidence from a randomized clinical trial in patients with severe/critical aortic stenosis. Adoption of TAVR to populations beyond aortic stenosis, which was studied in the randomized trial, is not appropriate at the current time. However, in view of the promising results obtained in these limited population subsets, further randomized trials in other patient groups is strongly encouraged.

The target patient population for treatment of aortic stenosis with TAVR within the Medicare population will be limited to Medicare beneficiaries who are considered high-risk operative candidates or inoperable based on advanced age in combination with other clinical measures and/or the evaluation of the patient based on the STS Risk score (which is available at <http://www.sts.org/quality-research-patient-safety/quality/risk-calculator-and-models/risk-calculator>). Current evidence on transcatheter aortic valve replacement for aortic stenosis is limited to patients who are considered to have a poor prognosis without treatment and/or are at high risk if treated by conventional open heart aortic valve replacement. These patients carry a high mortality risk due to advanced age and/or the presence of concomitant illnesses. TAVR is not intended for use in Medicare beneficiaries who are considered acceptable operative candidates as defined by STS and ACC guidelines and the multidisciplinary team or in those patients with such advanced age and comorbidities that good clinical outcomes could not be achieved even with TAVR. Quality of life beyond one year following the procedure will be considered essential in deciding which patients will benefit from these procedures.

The multidisciplinary structural heart valve disease team, which includes the primary cardiologists, surgeons and interventional cardiologists, will be central in applying scoring systems to evaluate risk-benefit profiles in this diverse group of patients. The multidisciplinary team should have specific protocols for care related to pre-procedure assessment and screening. These protocols should be

implemented and executed jointly by the multidisciplinary team. These protocols will involve screening for the presence, degree, and severity of comorbidities, issues related to the aortic pathology that may affect outcome and identification of optimal strategies and other procedures that may be required to ensure good outcomes (e.g., the treatment of coronary obstructive lesions prior to the placement of a percutaneous TAVR). Such protocols and procedures should be contained in well-defined patient-care pathways. Adherence to these principles will not only prevent inappropriate use of these devices, but will ensure best patient outcomes and optimal device utilization.

4. Supporting medical and scientific information

a. Overview of the technology

Traditional aortic valve replacement surgery through a median sternotomy or a more limited minimally invasive approach has been the mainstay of treatment for valvular heart disease. In general, when used in experienced centers with qualified surgeons, the results of TAVR use have been excellent - improving morbidity and mortality as compared with medical therapy. This technology is timely as invasiveness and recovery time for the patient have recently become an issue. Since the introduction of minimally invasive and catheter-based therapies, patients have wanted less invasive options for all types of medical procedures including general surgical, orthopedic, spinal, and urologic operations with the goal of decreasing morbidity and mortality and shortening recovery time. TAVR offers such a technology and has been proven to be beneficial for highly selected patients with aortic valve stenosis.

TAVR utilizes a bioprosthetic valve that is inserted using a catheter-based technology. The delivery can be accomplished using either a percutaneous (through the peripheral artery) or a transapical (directly inserting the device through the apex of the heart) approach. Additional approaches may include a transaortic approach through a limited sternotomy. Either option is less invasive than traditional open heart surgery, which is currently the standard for aortic valve repair and replacement.

b. Estimated number of patients who qualify for the procedures

At this time, less than 5,000 transcatheter invasive aortic valve replacement procedures are anticipated to be performed per year in the United States, with approximately 2/3 of these procedures believed to be from an endovascular approach and 1/3 from an open thoracic approach. The procedure will be performed on patients who meet rigorous selection criteria that are based on advanced age and comorbidities and who are considered to be inoperable or high risk operative candidates. Selection criteria will be based on the experience gained from the Placement of Aortic Transcatheter Valve Trial (PARTNER) Trial and on FDA labeling. As these emerging techniques continue to evolve and the number of clinical trials increases, utilization of these procedures over time is expected to increase albeit in a controlled fashion based on evolving evidence from further clinical trials or on evaluation of data from the TVT registry and consensus building among involved stakeholders.

c. General background

To date, one clinical trial has been conducted to evaluate the use, safety, and effectiveness of transcatheter aortic valve insertions utilizing either a percutaneous or a transapical approach. The PARTNER trial has provided data that the treatment is safe and effective for a select group of

patients. In addition, the trial data underscored the importance of a controlled environment for delivery of these procedures. In order to ensure safe and effective practices for TAVR insertions, it is important to implement guidelines that ensure the procedures are performed in specialized heart centers with specialized equipment, sufficient volume, and properly trained and credentialed multidisciplinary teams that have agreed upon joint decision making and co-management principles involving the selection and technical aspects of treatment of patients at risk. Continued review of data and outcomes with necessary refinements to guidelines and protocols utilizing a joint TVT registry is felt to be essential.

d. Basic research

The PARTNER clinical trial has provided some initial data on the protocols and guidelines that need to be followed to provide safe, effective and appropriate treatment of aortic valve stenosis in high-risk and inoperable patients. This trial has shown that TAVR provides a safe and effective treatment for an otherwise untreatable patient population. The technology has only been shown to be effective in treating aortic stenosis in select high risk patient populations in a well-defined, controlled environment. In addition the clinical trials in the U.S have shown that it is critical to have the necessary advanced equipment and trained multidisciplinary providers in specialized centers to ensure good clinical outcomes utilizing the TAVR technology.

e. The devices

The TAVR devices are all similar in that they allow for transcatheter deployment of a bioprosthetic aortic valve utilizing either a percutaneous or transapical approach. There are approximately 10 different companies involved in the development of transvascular aortic valve insertion devices. Some of the companies that are involved the development of TAVR devices include the following: CoreValve ReValving System (Medtronic, Inc.), Direct Flow Medical Valve (Direct Flow Medical, Inc.), Edwards SAPIEN and SAPIEN XT (Edwards Lifesciences, LLC), Melody Valve (Medtronic, Inc.), Portico transcatheter aortic heart valve (St. Jude), and Lotus Valve (Sadra Medical). None of these products have received FDA approval for aortic valve replacement. The CoreValve ReValving System and the Edwards SAPIEN valve are currently being evaluated by clinical trial in the United States.

f. Clinical experience

The pivotal PARTNER trial has received a great deal of interest. Specific details about patient selection, protocols used, endpoints, and statistical evaluation are crucial. The PARTNER trial consisted of two parallel trials that enrolled the highest-risk patients ever seen in any cardiovascular trial by virtue of their age and severity of their comorbidities: 1) PARTNER Cohort A, which randomized high-risk surgical patients to either traditional aortic valve replacement or to TAVR by either a transfemoral or transapical approach; and 2) PARTNER Cohort B in which patients who were inoperable were randomized to either a TAVR by a transfemoral approach or to conventional medical therapy, which typically consisted of balloon aortic valvuloplasty. Screening required an evaluation by two experienced cardiac surgeons who agreed on the surgical risk using the STS Predicted Risk of Mortality score. These standards proved to be highly selective, with approximately one quarter to one third of screened patients subsequently enrolled. The primary endpoint was death from any cause at one year.

The results of PARTNER Cohort B have recently been published. In Cohort B, 358 patients were deemed unsuitable for conventional aortic valve replacement because of predicted probability of 50% mortality or at risk for a serious irreversible complication within 30 days. Within this population, at one year, all-cause mortality with TAVR was 30.7% as compared to 50.7% with medical therapy (hazard ratio: 0.55, 95% confidence interval: 0.40 to 0.74). Despite the marked improvement in survival and event-free survival, there were some significant safety hazards noted: a higher incidence of major strokes (5.0% versus 1.1%) as well as increased major vascular complications (16.2% versus 1.1%) with TAVR. Both of these complications may impact early and longer-term outcome adversely. As such, long term outcomes analysis will be required.

The results of the Cohort B evaluation were received enthusiastically; however, they must be applied cautiously. First, they can be applied only in patients similar to those in the study (i.e., those patients deemed to be inoperable). Second, they are the result of treatment by very experienced operators working as a heart team in a hybrid operating room or similar facility with a specific device and do not necessarily apply to other devices.

The preliminary results of the PARTNER Cohort A trial have also been published. The primary endpoint of the trial was met: TAVR was found to be noninferior to aortic valve replacement for all-cause mortality at one year (TAVR versus aortic valve replacement, 24.2% versus 26.8%, respectively, $p_{0.001}$ for noninferiority). Death at 30 days was lower than expected in both arms of the trial: TAVR mortality (3.4%) was the lowest reported in any series, despite an early generation device and limited previous operator experience.

Aortic valve replacement mortality (6.5%) was lower than the expected operative mortality (11.8%). However, both TAVR and aortic valve replacement were associated with important but different peri-procedural hazards: major strokes at 30 days (3.8% versus 2.1%, $p_{0.20}$) and 1 year (5.1% versus 2.4%, $p_{0.07}$), and major vascular complications were more frequent with TAVR (11.0% versus 3.2%, $p_{0.001}$). Major bleeding (9.3% versus 19.5%, $p_{0.001}$) and new onset atrial fibrillation (8.6% versus 16.0%, $p_{0.001}$) were more frequent with aortic valve replacement.

The trial investigators concluded that “a multidisciplinary valve team approach benefits patients and is recommended for all future valve centers.” **These results cannot be extrapolated to evaluate the outcome of this procedure in patients who are acceptable candidates for conventional aortic valve replacement.** For this to occur, more randomized controlled studies will need to be performed.

The 30-day mortality in PARTNER Cohort A (3.4%) and PARTNER Cohort B (5.2%) is better than the published European registry mortality (8.5%) (21–23). This raises questions about the “generalizability” of these trial results after commercialization in the United States. **Responsible diffusion of this technology with close monitoring of outcomes after commercialization will be critical to maintain these results.** The incidence of neurologic events (5.5% at 30 days, 8.3% at 1 year) and major vascular complications (11%) that occur in patients undergoing TAVR also needs to be addressed. The role of embolic protection, smaller delivery systems and post-procedure anticoagulation, remains to be determined.

g. FDA documentation

At this time, none of the TAVR devices have received FDA approval.

5. FDA information

At this time, none of the TAVR devices have received FDA approval.

6. Explanation of design, purpose, and method of using the item or equipment, including whether the item or equipment is for use by health care practitioners or patients

a. Establishment of regional centers of excellence for heart valve diseases

Criteria for centers performing interventional therapy in valvular and structural heart disease will be established through consensus building from STS, ACC and other interested parties. The availability of devices and reimbursement for those procedures should be limited to centers meeting those criteria.

In the case of TAVR, the specialized expertise, experience, imaging equipment, and facilities equipped to optimize outcomes are not available in all programs. Because of the myriad of specialists, imaging equipment, procedural facilities, and support infrastructure necessary to build a valve center, it is recommended that access to TAVR should not be universal and immediate but should be implemented in a controlled and regulated fashion. In the United States, many cardiac surgical centers and catheterization laboratories have a very low volume of structural heart disease cases. Outcomes for patients undergoing surgery for valvular heart disease have clearly been demonstrated to be related to center procedural volume. The complexities of the management of valvular heart disease will require the infrastructure available only in regional referral centers with acceptable patient volume in valvular heart disease as established by the ACC and STS.

In order to create specialized regional centers, detailed lists of facilities and personnel experience in addition to pre- and post-procedural care protocols as well as management strategies for complications must be developed and then implemented.

b. Multidisciplinary heart teams

The concept of a multidisciplinary professional heart team has received increasing interest, beginning particularly with the **SYNTAX** (SYNTAX Study: TAXUS Drug-Eluting Stent Versus Coronary Artery Bypass Surgery for the Treatment of Narrowed Arteries) trial of patients with advanced coronary artery disease. In the SYNTAX trial, following angiography, the interventional cardiologist and cardiovascular surgeon reviewed the angiographic films together in the context of the clinical setting. If the patient was deemed to be an acceptable candidate for either procedure, both physician and surgeon—ideally together—would interview both patient and family to formulate an optimal plan. This “heart team” concept has been endorsed and recommended in the recent European Society of Cardiology/European Association for Cardio-Thoracic Surgery Guidelines on Myocardial Revascularization and should become the standard of care.

The heart team concept has been extended to treatment of valvular heart disease. In the PARTNER Trial, the pivotal U.S. trial of a new device for TAVR, patients are routinely

evaluated by “partners” of cardiologists and surgeons together to determine patient eligibility and optimal treatment strategy. This requires pre-procedural evaluation in valvular heart disease clinics, multidisciplinary team conferences, joint performance of the procedure, as well as postoperative care. Such a heart team will be even more critical as the issues with structural heart disease become more complex, the treatment expands to more centers, and new technology is applied outside of the constraints of randomized clinical trials. The success of this team concept has been demonstrated in heart transplant centers in which patient treatment decisions and care are managed by heart failure cardiologists, transplant and ventricular assist device surgeons, experts in immunosuppression, as well as specialists in echocardiography and in anesthesia; all of whom collaborate as a multidisciplinary team. Key members of the multidisciplinary team for structural heart valve disease management include primary cardiologists, interventional cardiologists, cardiac surgeons, noninvasive and heart failure cardiologists, echocardiographers and cardiac imaging specialists, cardiac anesthesiologists, nurse practitioners, physician assistants, research coordinators, administrators, dietary and rehabilitation specialists, and social workers. Each component will need to develop and implement specific protocols depending on the individual patient and specific technical procedure.

The multidisciplinary team will be central in applying a standardized scoring system to evaluate risk-benefit profiles in this diverse group of patients. The patient’s values and goals need to be central in benefit-risk assessment and treatment decisions.

Primary cardiologists

The primary cardiologists typically have seen these patients longitudinally over the course of their diseases and have a unique perspective of patient and family dynamics. These physicians coordinate care, ensure complete evaluation, order and evaluate diagnostic studies, implement medical care, and ensure involvement of patients and families in the decision-making process. Primary cardiologists also resume care of the patient after the procedure and need to be cognizant of the follow-up needs and protocols; accordingly, these individuals are an essential component of the heart team to enhance patient-centered care. The patient’s values and goals need to be central in benefit-risk assessment and treatment decisions.

Cardiac surgeons and interventional cardiologists

Cardiac surgeons and interventional cardiologists who have had appropriate training and experience as defined by the joint STS/ACC/SCAI consensus statement being developed will work together in the treatment and management for transcatheter valve insertions patients. Both will have responsibility in the technical aspect of the procedure and will share in the case volume and decision-making about which patients are appropriate for the use of this technology. Both will need to possess adequate catheter based skills as well as surgical skills to accomplish the technical aspects of the device deployment, knowledge of the criteria for patient selection to assist in the decision making process, and adequate knowledge and support to provide post operative patient management. Each will have a responsibility to the other to ensure that their decision making, technical ability, and expertise in using the device is done in an appropriate and safe manner for Medicare Beneficiaries. Minimum ongoing case volumes will be established by STS/ACC/SCAI and monitored to ensure that interventional cardiologists and surgeons continue to have the required skills to participate in the use of this technology.

Echocardiographers and imaging specialists

Echocardiography will be critical, with collection of standardized definition sets. Mandatory imaging modalities necessary for a structural heart disease program include 2- and 3-dimensional transthoracic and transesophageal echocardiography, vascular computerized tomography with 3-dimensional reconstruction, cardiac magnetic resonance imaging, diffusion weighted magnetic resonance imaging of the brain, and transcranial Doppler imaging. An important screening component for TAVR involves 3-dimensional reconstruction of the aortoiliac vasculature using multislice computerized tomography (MSCT). The current aortic transvalvular device delivery sheaths are large, ranging from 18- to 24-Fr in diameter. Although they are becoming smaller in diameter, access remains an issue. Accordingly, it is essential to identify absolute arterial diameters and specific abnormalities such as severe calcification or tortuosity of the aortoiliac vascular tree that may dictate an alternative access route.

Heart failure specialists

An increasing number of patients with advanced valvular heart disease have a component of left ventricular dysfunction. For patients with aortic stenosis, left ventricular dysfunction may render the assessment of the severity of the aortic stenosis difficult, thus complicating decision making about the need for or performance of a procedure. In addition, heart failure specialists will need to help assess the potential for reversibility of left ventricular dysfunction following TAVR. Identification of appropriate patients with aortic stenosis and heart failure who may benefit from a catheter-based approach is best accomplished by consultation with heart failure specialists.

Cardiac anesthesiologists

The cardiac anesthesiologist determines the most appropriate anesthesia and monitoring techniques for the patient and provides technical expertise in advanced imaging. Like interventional cardiologists and cardiac surgeons, cardiac anesthesiologists will need to form dedicated teams to safely apply this technology to a high risk Medicare beneficiary population.

c. Establishment of a national registry for valvular heart disease (See TVT Registry summary from 9/22/2011 application supplemental documents)

Mandatory reporting to the STS/ACC TVT registry will monitor post-market surveillance, long-term outcome measurement, and comparative effectiveness research. The registry will be developed by the STS and ACC in conjunction with input from the specialty societies and other relevant stakeholders.

Both the STS and ACC maintain large clinical databases that collect and analyze outcomes of surgical and catheter based procedures. An initial pilot project, the ACCF/STS Collaboration on the Comparative Effectiveness of Revascularization Strategies (ASCERT), linking the two clinical databases to administrative databases including the Social Security Death Master File (SSDMF) and Centers for Medicare & Medicaid Services Medicare Provider and Analysis Review (MedPAR) data in patients with coronary artery disease is currently under way. Another pilot project highlighting successful linkage of the STS database to the SSDMF and reporting 1-year survival after cardiac surgery was published in 2010. A similar linking of clinical and administrative databases to perform post-market surveillance, assess long-term patient-centered outcomes research, and perform comparative effectiveness research and cost effectiveness for all

patients with valvular heart disease is crucial. This linkage needs to involve shared modules to avoid duplicate data entry.

One model currently being utilized for tracking outcomes of patients receiving left ventricular assist devices—the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) registry—should be considered for transcatheter valves. The construction of these linked outcome databases is critical to adequately assess the impact of transcatheter valves on the clinical outcomes of patients with valvular heart disease. It is also important to consider the use of common data forms, definitions, and reporting processes in different countries. Initial discussions are under way to determine the feasibility of linking various national registries together to establish a truly global database. Transcatheter and surgical valve therapy provide an optimal initial platform to foster this linkage. This will facilitate evaluation and interpretation of the results of ongoing and future planned studies. Additionally, it will enable regulatory trials for the FDA by allowing better utilization of global data when considering new device trial submissions and will enhance payer understanding of the best decision making for application of these technologies. This will require that the different international societies become more fully engaged and integrated.

d. Training and credentialing criteria

Operator training is a crucial component for treating structural valvular heart disease using a TAVR approach. Construction of a training curriculum is essential. Formation of criteria for fellowship training programs as well as postgraduate training with appropriate experience for adequate patient care leading to guidelines for credentialing will be established by the STS/ACC/SCAI in a consensus statement currently under development.

There will be minimal case volume requirements for catheter based and surgical based approaches. Both the cardiologist and surgeon will have to have hybrid training involving catheter based and surgical skills in order to establish a TAVR program. Following the establishment of a program all members of the multidisciplinary team will need to maintain minimal volume requirements for continued participation and will be monitored on an ongoing basis to ensure acceptable outcomes as defined by ACC/STS/SCAI criteria. The institutional structural requirements and cardiology/cardiac surgeon volume and outcomes criteria for TAVR will be developed using the CMS criteria for heart transplant centers as a template. The criteria will be based on retrospective analyses of outcomes.

7. Benefits and relevance of procedure to the Medicare population

a. An explanation of the relevance of the evidence selected

Prior to the TAVR technology, there were Medicare beneficiaries who were not considered to have any effective treatment for their aortic stenosis other than medical management. Historically they have had poor outcomes. Often they were denied operative intervention based on advanced age and other comorbidities. Based on the results of the PARTNER Trial, TAVR now offers an effective alternative to medical management with acceptable morbidity and mortality for this elderly population whose quality of life and longevity was severely compromised by their aortic stenosis.

The pivotal PARTNER trial has received a great deal of interest. Specific details about patient selection, protocols used, endpoints, and statistical evaluation are crucial. The PARTNER trial consisted of two parallel trials that enrolled the highest-risk patients ever seen in any cardiovascular trial by virtue of their age and severity of their comorbid conditions: 1) PARTNER Cohort A, which randomized high-risk surgical patients to either traditional aortic valve replacement or to TAVR by either a transfemoral or transapical approach; and 2) PARTNER Cohort B in which patients who were inoperable were randomized to either a TAVR by a transfemoral approach or to conventional medical therapy, which typically consisted of balloon aortic valvuloplasty. Screening required an evaluation by two experienced cardiac surgeons who agreed on the surgical risk using the STS Predicted Risk of Mortality score. These standards proved to be highly selective, with approximately one quarter to one third of screened patients subsequently enrolled. The primary endpoint was death from any cause at one year.

The PARTNER Cohort A trial has equally important implications. The primary endpoint of the trial was met, with TAVR found to be noninferior to aortic valve replacement for all-cause mortality at one year (TAVR versus aortic valve replacement, 24.2% versus 26.8%, respectively, $p_{0.001}$ for noninferiority). Death at 30 days was lower than expected in both arms of the trial: TAVR mortality (3.4%) was the lowest reported in any series, despite an early generation device and limited previous operator experience. Aortic valve replacement mortality (6.5%) was lower than the expected operative mortality (11.8%). Furthermore, both TAVR and aortic valve replacement were associated with important but different peri-procedural hazards: major strokes at 30 days (3.8% versus 2.1%, $p_{0.20}$) and 1 year (5.1% versus 2.4%, $p_{0.07}$), and major vascular complications were more frequent with TAVR (11.0% versus 3.2%, $p_{0.001}$). Major bleeding (9.3% versus 19.5%, $p_{0.001}$) and new onset atrial fibrillation (8.6% versus 16.0%, $p_{0.001}$) were more frequent with aortic valve replacement. The trial investigators also concluded that “a multidisciplinary valve team approach benefits patients and is recommended for all future valve centers.” These results cannot be extrapolated to evaluate the outcome of this procedure in patients who are acceptable candidates for conventional aortic valve replacement. For this to occur, more randomized controlled studies will need to be performed.

The 30-day mortality in PARTNER Cohort A (3.4%) and PARTNER Cohort B (5.2%) is better than published European registry mortality (8.5%) (21–23). This raises questions about the “generalizability” of these trial results after commercialization in the United States. Responsible diffusion of this technology with close monitoring of outcomes after commercialization will be critical to maintain these results. The incidence of neurologic events (5.5% at 30 days, 8.3% at one year) and major vascular complications (11%) that occur in patients undergoing TAVR also needs to be addressed. The role of embolic protection, smaller delivery systems and post-procedure anticoagulation, remains to be determined.

b. Rationale for how the evidence selected demonstrates the medical benefits for the target Medicare population

Medicare patients with aortic stenosis who were previously considered inoperable or high-risk operative candidates for aortic valve surgery now have access to safe and effective therapies for previously untreated aortic valve stenosis. The safe and appropriate application of TAVR in the Medicare population should be limited to structural heart valve centers of excellence with appropriately credentialed surgeons and interventional cardiologists, cardiac anesthesiologists, and other members of the identified multidisciplinary team. The results of the PARTNER Trial

in such established centers have demonstrated that this technology can be used in a high risk Medicare population with acceptable results.

c. Information that examines the magnitude of the medical benefit

The TAVR technology will benefit a select portion of the Medicare population. It is currently estimated that 5000 minimally invasive aortic valve replacement procedures will be performed per year. Of those procedures, it is estimated that approximately 2/3 (3300) of those patients will be Medicare patients.

d. Reasoning for how coverage of the item or service will help improve the medical benefit to the target population

Directed coverage of the TAVR procedures will allow previously untreated or untreatable Medicare patients with a diagnosis of aortic stenosis to receive safe and effective treatment of their disease that has not been available until now. This allows the target Medicare population with aortic stenosis that was previously untreatable due to the patient being inoperable or high risk a treatment option to either prolong life and/or improve their quality of life.

8. A description of any clinical trials or studies currently underway that might be relevant to a decision regarding coverage of the item or service

PARTNER Trial (NCT00530894) - ongoing

A robust knowledge of the current scientific literature is mandatory to place this technology in perspective. Data from multiple single-center series and national and commercial registries are available for transcatheter aortic and mitral valve procedures. Randomized clinical trials represent the highest form of evidence-based medicine and form the backbone of regulatory approval and instructions for use. The results of the PARTNER pivotal trial of transcatheter aortic valves have been published. A committee of the cardiac specialty societies involved will subsequently convene and publish an expert consensus statement in 2011. Evaluation of some of the data from this randomized trial is important as it affects the process of development and implementation of these technologies. In addition to the PARTNER Trial there are two other trials underway in the US involving TAVR (please reference www.clinicaltrials.gov):

Medtronic CoreValve U.S. Pivotal Trial

Repositionable Percutaneous Replacement of Stenotic Aortic Valve Through Implantation of Lotus™ Valve System (REPRISE I). This study is not yet open for participant recruitment. Boston Scientific Corporation

9. Use of drug or device subject to FDA regulations and the status of the current FDA regulatory review

There are currently multiple companies involved in the development of transvascular aortic valve replacement. Some of the companies that are involved the development of TAVR devices include the following: CoreValve ReValving System (Medtronic, Inc.), Direct Flow Medical Valve (Direct Flow Medical, Inc.), Edwards SAPIEN and SAPIEN XT (Edwards Lifesciences, LLC), Melody Valve (Medtronic, Inc.), Portico transcatheter aortic heart valve (St. Jude), and Lotus Valve (Sadra Medical).

None of these products have received FDA approval for aortic valve replacement. The CoreValve ReValving System and the Edwards SAPIEN valve are currently being evaluated by clinical trial in the United States.

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Edwards Lifesciences Percutaneous Aortic Heart Valve

The Edwards Lifesciences percutaneous aortic heart valve (Edwards Lifesciences, Irvine, CA, USA) is the Cribier-Edwards percutaneous aortic bioprosthesis. The prosthesis is an equine pericardium tricuspid valve mounted on a stainless steel stent (Figs. 62a & 62b). The original 23-mm prosthesis is crimped with the crimper device and advanced following a 22-mm Numed balloon catheter compatible with a 24F sheath. The device can be advanced retrogradely from the femoral vein with a transeptal approach across the mitral valve to the left ventricle or antegradely from the femoral/iliac or subclavian artery to the ascending aorta. The positioning and delivery are supported by angiography and echocardiography and a short interval of rapid pacing at 220 bpm to produce transient blood-flow reduction. The postoperative gradients and aortic valve areas of this investigational prosthesis in high-risk/non-operative patient candidates have been reported by Dr. Alain Cribier (Paris), and Dr. John Webb (Vancouver). The Paris series was conducted with 23-mm prostheses, whereas the Vancouver series was conducted with 26-mm prostheses. The first human implant was performed in Paris in April of 2002 in a feasibility study of compassionate patients. The potential complications are paravalvular leak following native calcific valve dilatation and prosthesis placement, cerebrovascular accident, and cardiac tamponade.

CoreValve Percutaneous Pericardial Aortic Valve

The CoreValve percutaneous pericardial aortic valve (CoreValve, Irvine, CA, USA) is a bovine pericardial valve mounted on a self-expanding nitinol stent. The prosthesis is implanted via the retrograde approach. The prosthetic frame (stent) is manufactured by laser cutting of a nitinol metal tube with a length of 50 mm. The lower part has a high radial force to push aside the calcified leaflets and avoid recoil, the middle part is constrained to avoid coronaries and carries the valve, whereas the upper part expands for fixation in the ascending aorta and exits the system. The actual valve inner diameter is 21 mm to 22 mm. The valve is delivered via a 25F catheter, which houses the stent in the distal part. The stent deployment is retrograde via a surgical cut-down of the common iliac artery. The procedure is performed currently under general anesthesia with transesophageal echocardiography (TEE) guidance and femoral-femoral partial cardiopulmonary bypass.

ENABLE™ Aortic Bioprosthesis, Model 6000

The ENABLE™ Aortic Bioprosthesis (3F Therapeutics, Lake Forest, CA, USA) consists of a 3F Aortic Bioprosthesis, Model 1000 that has been mounted into a self-expandable frame made from Nitinol temperature memory alloy (Fig. 65). It is malleable at 0°C to 5°C, which allows easy contraction of the diameter for quick insertion into the aortic root orifice that remains after resection of the diseased aortic valve on cardiopulmonary bypass. Above 20°C, the frame or stent expands to the given diameter of the valve size, the radial force being sufficient to maintain the position of the valve. Deployment times are less than 3 minutes, with the attendant decrease in ischemic and cardiopulmonary bypass times

ENTRATA™ Transventricular Aortic Bioprosthesis, Model 7000

The ENTRATA™ transventricular aortic bioprosthesis (3F Therapeutics, Lake Forest, CA, USA) consists of a tubular structure assembled from three equal sections of equine pericardial material preserved in glutaraldehyde (Fig. 66). The structure incorporates commissural tabs made from sections of pericardium anchored to the posts of the stent. The stent is manufactured from SMLS 316L vacuum melted extruded stainless steel tubing. Annealing of this stent allows compression and subsequent dilatation when within the aortic root. The aortic valve is dilated by way of the apical transventricular delivery system. The bioprosthesis is delivered antegradely through the apical transventricular catheter system into the ventriculo-aortic junction. The bioprosthetic valve is formulated in sizes 19 mm to 29 mm in increments of 2-mm diameters.

Sadra Percutaneous Pericardial Aortic Valve

The Sadra Percutaneous pericardial aortic valve (Sadra Medical, Campbell, CA, USA) is a self-expanding pericardial bioprosthesis on a nitinol stent. The prosthesis is designed for retrograde implantation and can be repositioned, as indicated. The bioprosthesis has an outer dynamic seal to prevent periprosthetic leak.

Nanotechnology Approaches to Percutaneous Aortic Valve

Prostheses based on nanotechnology are in the investigational stage. The AorTx (AorTx, Palo Alto, CA, USA) concept is one of these for percutaneous aortic valve replacement (Fig. 67). Another of these is the Palmaz-Bailey prosthesis composed completely of nitinol. These nitinol leaflets have the capacity for endothelial overgrowth.

Corazón Percutaneous Aortic Valve Repair (PAVR) System

The Corazón PAVR system (Corazón Technologies, Menlo Park, CA, USA) is designed for isolated demineralization of the aortic valve. The process incorporates gentle mechanical agitation and demineralization lavage at a low pH with hydrochloric acid and controlled pathways for simultaneous lavage of the aortic valve, solution neutralization, and aspiration. The percutaneous device consists of a flexible, multi-lumen catheter for percutaneous navigation, soft tip for placement into the left ventricle (LV), and a balloon for occluding the LV outflow tract below the aortic valve, an expandable central lumen with temporary aortic valve to enable beating heart aortic valve treatment, and aortic isolation of treatment using a compliant bell designed to conform to the shape of the aortic valve cusps.

10. References

(See TAVR Research Bibliography summary from 9/22/2011 application supplemental documents)

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