

March 13, 2013

The Honorable Margaret A. Hamburg, MD
Commissioner
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

**Re: Circulatory System Devices Panel of the Medical Devices Advisory Committee Meeting
Announcement; Notice of Meeting - Pre-Market Approval Application from Abbott
Vascular Inc. for the MitraClip System**

Dear Dr. Hamburg:

The American College of Cardiology (ACC) and The Society of Thoracic Surgeons (STS) are pleased to submit comments in response to the pre-market approval application of Abbott Vascular Inc. with respect to the MitraClip System and its use in patients who are considered too high risk for open mitral valve surgery. Such patients are classified as “inoperable”.

STS is a not-for-profit organization representing more than 6,600 surgeons, researchers, and allied health care professionals worldwide who are dedicated to providing patient-centered high quality care to patients with chest and cardiovascular disease, including heart, lung, esophagus, transplantation, and critical care. The mission of the Society is to enhance the ability of cardiothoracic surgeons to provide the highest quality patient care through education, research, and advocacy.

The American College of Cardiology is a 43,000-member nonprofit medical society composed of physicians, nurses, nurse practitioners, physician assistants, pharmacists and practice managers, and bestows credentials upon cardiovascular specialists who meet its stringent qualifications. The ACC is a leader in the formulation of health policy, standards and guidelines, and is a staunch supporter of cardiovascular research. The College provides professional education and operates national registries for the measurement and improvement of quality care.

The STS and ACC have forged a partnership to provide professional leadership, patient advocacy, and guidance to the government during the current era of novel technology development and dispersion in the field of transcatheter valve therapy. We appreciate the opportunity to furnish input to the Food and Drug Administration (FDA) and the Circulatory System Devices Panel of the Medical Devices Advisory Committee on this specific important new technology, the MitraClip that is the subject of FDA review.

The STS and ACC defer to the expert panel and the FDA to evaluate the totality of evidence of efficacy and safety to subsequently make decisions regarding regulatory approval of the MitraClip technology. Our role is to provide the panel and FDA with the background on key issues related to these patients and how the professional societies have recently taken on major responsibility in the realm of the rational dispersion of new technology, regulatory reform, device surveillance, patient access to new treatments, monitoring and improvement of the quality of care, and further research. These expanded responsibilities and accountability of STS and ACC are relevant to the potential outcomes of the panel and FDA review of the MitraClip technology.

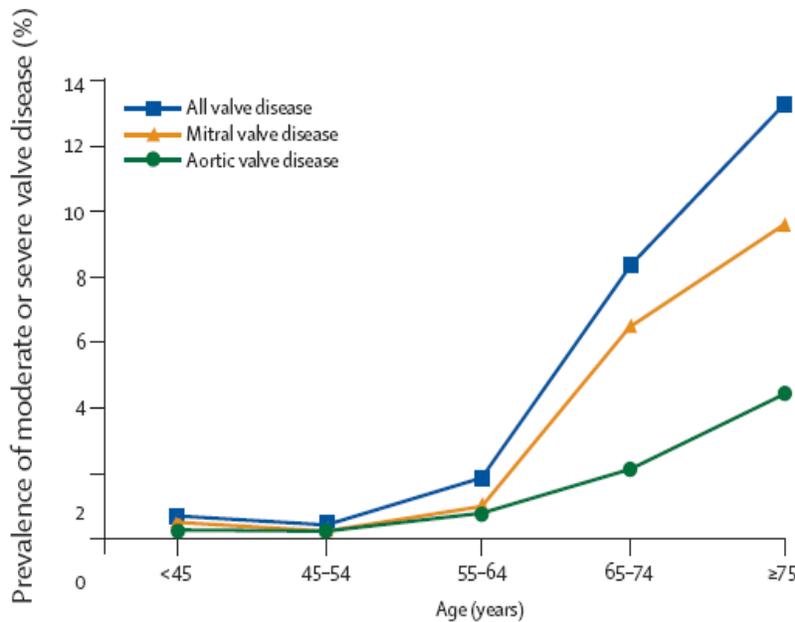
Our remarks will address the following questions:

1. Is mitral regurgitation a common, serious, and severe disease in the USA? Are new treatment options needed?
2. How are members of ACC and STS involved in the care for these patients?
3. How do the ACC and STS as organizations each provide leadership, clinical guidance, and education/training related to transcatheter therapies for valvular heart disease?
4. What is the potential role of the STS-ACC TVT Registry with the MitraClip System?

Is mitral regurgitation a common and severe disease in the US? Are new treatment options needed?

Valvular heart disease is a major source of mortality and morbidity. The success in eradication of acute rheumatic fever and consequent dramatic reduction of rheumatic heart valve disease are a major landmark of success in the management and prevention of cardiovascular disease. Yet in this century degenerative and functional abnormalities of cardiac valves have increased as our demographics shift. These disorders often occur in older individuals with multiple comorbidities and they are major drivers of the increased frequency of congestive heart failure and atrial fibrillation. They produce profound reductions in the quality and length of life, and represent major challenges in prevention and medical management.

Mitral regurgitation (MR) is the most common severe adult valvular heart disease in the United States. Its prevalence increases dramatically as the population ages to an extent that is even greater than aortic stenosis (see figure from Lancet 2006; 368:1005-11). Aortic stenosis especially in the elderly has received



much attention with the development of transcatheter aortic valve replacement (TAVR) and its approval by the FDA. No transcatheter option exists for those afflicted with MR. One in ten Americans who are 75 years of age or older have moderate to severe MR.

MR is a complex valve dysfunction due to the malfunction of the normally orderly dynamic 3-D mitral valve complex that is composed of “many moving parts” including valve leaflets, a dynamic annulus, multiple chordae tendinae, and papillary muscles. Intertwined with the

function of this valve complex is left ventricular function that, unlike aortic valve function, intrinsically impacts on the normal absence of MR as well as creating severe MR when the LV has regional or global dysfunction. Finally, the diagnosis and quantification of mitral regurgitation is not straightforward. The day-to-day variation in the degree of MR may be substantial. The quantification of MR utilizes a composite approach of echocardiographic and Doppler techniques. The American Society of Echocardiography (ASE) has established standards for the acquisition, interpretation, and reporting of valvular abnormalities including mitral regurgitation.¹

The conventional treatment for severe MR has been surgical mitral valve repair or replacement which yields excellent long-term outcomes and low operative risks when performed by skilled and experienced surgeons with their team. Increasingly, it has become apparent that a significant number of patients are ineligible for these surgical approaches due to excessive risks, inability to recover from surgery, and persistent symptoms related to left ventricular dysfunction, especially in functional mitral regurgitation. These patients are often older, frequently have multiple comorbidities, and may be frail by their intractable symptoms. Medical management may be maximized, but many patients remain severely symptomatic, have recurrent hospitalizations, and suffer markedly lower health status and poor quality of life. Thus, there is a clinical justification to develop and evaluate new approaches to the treatment MR and to initially target those who do not have other options or who have failed conventional approaches.

Recent clinical trials in the US, Canada, Europe, and other countries have demonstrated the potential for a new treatment option of transcatheter mitral valve repair with the MitraClip System. Randomized trial data, as well as prospective and observational data, have been published dealing with this specific valve technology. The ACC and STS eagerly await the review and recommendations from the expert panel convened to evaluate all data related to the MitraClip System as applied to patients who are deemed too high risk for open mitral valve surgery.

How are specialists involved in the care for these patients?

Patients who have severe MR and conditions that make open surgery not feasible require a comprehensive, longitudinal, well-integrated, and sophisticated approach from the time of diagnosis onward. In the last decade, clinical trials with the MitraClip technology have helped illustrate the roles of cardiologists and cardiac surgeons in the care of these patients and the special skills required.

The majority of patients who have suspected or identified MR will be referred to a cardiologist by other clinicians. The diagnosis and characterization of MR have been transformed by echocardiography, which allows visualization of relevant structures and a non-invasive assessment of the pressure and flow characteristics. The diagnosis, quantification, and classification of MR are performed by cardiologists and often involve the participation of imaging specialists, especially the echocardiographer. Echocardiographers are critical in not only evaluating patients for MitraClip, but they also participate in the procedure and follow-up of these patients. Furthermore, members of the heart team increasingly collaborate to assess comorbidities and the barriers to patient's recovery from potential surgery and similarly invasive procedures. As with the evaluation of patients for TAVR, the heart team must perform a comprehensive evaluation and integrate much data, including the patient's preferences and life goals, into a recommendation as to which of the available therapies —open surgery, transcatheter therapy, or medical therapy — are reasonable options for individual patients. In addition, heart failure specialists play an important role in ensuring that these patients are properly evaluated and are provided with subsequent treatments appropriate to patients with advanced heart failure. Finally, interventional cardiologists serve

¹ Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr* 2003;16:777-802.

as key members of the team evaluating these patients, performing the intervention, and caring for the patient post-procedure.

Cardiac surgeons play an important role in screening patients for the MitraClip. Surgical consultation is necessary to determine which patients can tolerate open surgical repair or replacement with an acceptable risk level. In medical centers participating in MitraClip clinical trials, the role of surgeons has expanded into anatomic evaluation of mitral valve pathology, screening for patients who are not surgical candidates, and, in a few centers, performing the MitraClip procedure with their interventional cardiology colleagues. This is an opportunity for further development of the “heart team” concept that is now integral to TAVR and many programs’ coronary intervention decision-making.

The concept and re-organization of clinicians to provide a collaborative approach to the care of patients with valvular heart disease has clearly emerged in the last five to 10 years and continues to spread to additional major medical centers. From the previous description of current practice in the evaluation and treatment of mitral regurgitation patients, it is clear that this team model applies here, as well as for patients with aortic stenosis. The concept is also in use in heart transplant centers. In these regionally located, highly specialized centers, patient treatment decisions and care are managed by experts in heart failure, transplantation, ventricular assist devices, immunosuppression, echocardiography, cardiac catheterization, and anesthesia. The mitral heart team consists of primary cardiologists, interventional cardiologists, cardiac surgeons, heart failure cardiologists, echocardiographers and other cardiac imaging specialists, cardiac anesthesiologists, nurse practitioners, physician assistants, research coordinators, administrators, dietary and rehabilitation specialists, and social workers. Each component of the care team will need to develop and implement specific protocols, depending on the individual patient and specific technical procedure. Both the STS and ACC have multiple examples of promoting this model and working with additional medical specialty societies to ensure a consistent approach.

How do the ACC and STS as organizations provide leadership, clinical guidance, and education/training related to transcatheter therapies for valvular heart disease?

Cardiovascular specialists aim to provide the highest quality patient care. One component of that high quality care is ensuring responsible disbursement of this new technology. Transcatheter mitral valve repair is an advanced, sometimes complex, and specialized procedure, requiring an increased level of interventional expertise and experience. To ensure rational and responsible dissemination of this new technology, government, industry and medicine will need to work in harmony. We look forward to this opportunity to work together to make high quality patient care available to the appropriate patient population in the appropriate setting from appropriately experienced operators conducting the necessary follow-up.

Opportunities to collaborate

The practice of cardiovascular medicine has changed dramatically over the last 10 years. The improvements in diagnostic imaging and technological advances have brought with them significant reductions in morbidity and mortality. Government, industry, and medicine have all played important roles in fostering the technologies and the climate that have allowed for these tremendous improvements in patient care. However, as these new technologies have emerged, government, industry and medicine have struggled with how best to disseminate and provide access to these new procedures. The ACC and STS believe that all three groups are important to this process and must come together to ensure appropriate availability and use. Responsible dissemination of a new technology requires input and collaboration between industry and the applicable specialty societies. The manufacturer is generally best equipped to educate physicians on the details of the specific device, while the applicable specialty society or societies are best equipped to educate physicians regarding the particular disease state and the various

therapies available for treatment of that disease, as well as to provide the framework for pre-procedural planning, procedural performance, and follow up. Government can facilitate these interactions and encourage collaboration among all affected parties. In these modern times, novel implantable devices like MitraClip require that the roles, relationships and supportive interactions between federal agencies and professional societies be revisited with a creative and pragmatic eye.

We believe it is important for the physician community to coordinate and collaborate in order to present a unified response to requests regarding a wide variety of issues. Here, as with transcatheter aortic valve repair, the organizations representing the various physician specialties involved in transcatheter aortic valve therapies (TAVR) have worked diligently to come together to ensure collaboration. Both STS and ACC recognize that transcatheter valve therapy is a hybrid of multiple very advanced medical disciplines, and as such, collaboration between those disciplines is critical. In 2011 the ACC and the Society for Thoracic Surgery (STS) released a high-level “Professional Society Overview” addressing transcatheter valve therapy that was published in both the *Journal of the American College of Cardiology*² and the *Annals of Thoracic Surgery*.³ This document set the stage for a series of clinical documents that addressing the issues critical to successful integration of TAVR into medical practice in the United State and including representation from a wide range of physician stakeholders⁴ As representatives of cardiologists, surgeons, interventional cardiologists, imaging specialists, and other members of the multidisciplinary heart team as noted below, these organizations are highly respected and trusted by the professionals who perform the services. Thus, documents drafted and reviewed by their peers will have great influence over behavior.

The ACC and STS strongly believe that the medical community has an important role to play in the dissemination of new technology. It is incumbent upon the physician community to act responsibly by setting forth guidelines as mentioned above, developing multidisciplinary teams with representation from all affected specialties, selecting appropriate patients, providing guidance regarding facility requirements, coordinating amongst itself to ensure providers have the necessary education and conducting effective follow-up and study.

Rational Dispersion of MitraClip

“Rational dispersion” of new transcatheter technologies for valvular heart disease has been a central theme of the ACC and STS for the past three years. This concept includes the introduction of the device into clinical situations that mimic as closely as possible those in the randomized clinical trial or registries as used for MitraClip. Transcatheter mitral valve repair should be considered one program, not just a procedure, with many similarities to a transplant program. Centers that perform MitraClip should have sufficient supporting infrastructure in terms of personnel and facilities to optimize the care of these patients and support programmatic excellence. The multidisciplinary heart team, as described above, must have significant experience in the management of patients with valvular and structural heart disease.

² Holmes DR, Jr., Mack MJ. Transcatheter valve therapy: a professional society overview from the American College of Cardiology Foundation and the Society of Thoracic Surgeons. *J Am Coll Cardiol* 2011;58:445–55.

³ Holmes DR Jr., Mack MJ. Transcatheter valve therapy: a professional society overview from the American College of Cardiology Foundation and The Society of Thoracic Surgeons. *Ann Thorac Surg* 2011;92:380-9.

⁴ [Tommaso CL](#), [Bolman RM 3rd](#), [Feldman T](#) et al. Multisociety (AATS, ACCF, SCAI, and STS) Expert Consensus Statement: Operator and Institutional Requirements for Transcatheter Valve Repair and Replacement, Part 1: Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol* 2012;59:2028-42. Holmes DR Jr., Mack MJ, Kaul S, Agnihotri A, Alexander KP, Bailey SR, Calhoon JH, Carabello BA, Desai MY, Edwards FH, Francis GS, Gardner TJ, Kappetein AP, Linderbaum JA, Mukherjee C, Mukherjee D, Otto CM, Ruiz CE, Sacco RL, Smith D, Thomas JD. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol* 2012;59:1200-54.

There must be access to substantial numbers of patients with MR to maintain procedure volume and cadence.

The specifics of patient selection, operator experience and skill requirement, institutional facility prerequisites, and hospital and clinician involvement in the STS-ACC TVT Registry have been comprehensively presented in multiple documents as it related to TAVR. The expert panel and the FDA can assume that these efforts will be similarly and immediately addressed by STS and ACC in the event of the approval of the MitraClip technology. Furthermore, we acknowledge the need to broaden the involvement of additional medical societies, including ASE, the Society for Cardiovascular Angiography and Interventions (SCAI), and the Heart Failure Society of America (HFSA). The following are some key background issues to be addressed in future expert consensus documents on the use of the MitraClip technology.

Patient selection

Careful patient selection is essential to achieving positive outcomes for any cardiovascular therapy. It is especially critical for novel therapies, such as transcatheter mitral valve repair. Physicians on the multidisciplinary heart team must work in concert with each other to determine whether individuals are appropriate candidates for this new procedure. Given the complexities of the procedure, patient selection is not a simple task. Many questions remain unanswered regarding specific patient selection criteria. Thus, it is important that FDA approval for the device be limited to those patients who fit the criteria where positive outcomes were demonstrated in the trials, namely those patients deemed inoperable for open mitral valve surgery. Determination of inoperability, by definition, requires direct involvement of a qualified cardiac surgeon member of the heart team. That said, it is equally important that the outcomes in other patient populations continue to be studied for the potential expansion of the new procedure for the other patients and incorporation in patient management care guidelines specifically for valvular heart disease.

Facility requirements

Today, many cardiac surgical centers and catheterization laboratories have a limited volume of structural heart disease cases. Based on the STS Database, 21,960 mitral valve repair and replacements were performed in 2011. When compared with the 166,816 coronary artery bypass grafts that were performed during that same time period, it is clear that few centers have a large volume of this service. Yet, studies indicate that outcomes for patients undergoing surgery for valvular heart disease have a direct relationship to center procedure volume. Given the complexity of these cases, it is important that facilities that would perform MitraClip have significant experience and adequate resources. Thus, the ACC and STS support development of centers with specialized expertise in MR and MitraClip. The level of complexity and resources required to perform MitraClip mean that not all facilities that wish to furnish the procedure should do so immediately following device approval. Similar to transplant centers, patients will benefit most from experienced centers that perform a comparatively substantial number of MitraClip procedures. The centers should initially have characteristics that match the criteria of those participating in the clinical trials. Patient access to such a specialized center is important with the caveat that MitraClip is typically not an urgent procedure requiring that there must be centers in close proximity.

The centers will also need to have a cardiac catheterization laboratory with the ability to integrate the 2D and 3D transesophageal echocardiograms (TEE) needed to optimally guide MitraClip.^{5,6} Because of the

⁵ Lang RM, Badano LP, Tsang W, Adams DH et al. EAE/ASE Recommendations for Image Acquisition and Display Using Three-Dimensional Echocardiography. J Am Soc Echocardiogr 2012;25:3-46

nature of the procedure, the interventional room needs to accommodate this equipment, the team performing general anesthesia, and the sterility needed for implanting a permanent cardiovascular device. There must be proximity and a process for emergency open cardiac surgery, although this need has been extremely low in clinical trials in the US and clinical practice outside of the US.

Additionally, post-procedure patient care requires access to personnel experienced with hemodynamic assessment and large-bore catheter and sheath vessel access issues. Given the host of potential issues and complications, cardiovascular intensive care units with experience in transcatheter therapy patients are best situated to care these patients with multiple comorbidities

Operator training and education

The ACC and STS support the division of training into two components: education regarding the disease and range of therapies and training on particular devices. Industry has specific regulatory requirements to train users on particular proprietary devices, and manufacturers are the ones with the best information regarding their particular devices. However, we firmly believe that it is the responsibility of the affected specialty societies to conduct the disease state and treatment options education. To that end, the ACC, STS, and others have developed such programs for TAVR and will continue to develop additional programs as needed for MitraClip. There is much still to learn, and thus, it is important that determinations regarding these requirements and guidelines be left to the professional societies for definition after a thorough review of all available evidence.

Post-procedure follow-up

Critical to learning about outcomes and patient safety is a mechanism for collecting data on patients who receive the procedure and have the devices implanted. Clinical trials can provide information on immediate outcomes and even short-term or intermediate follow-up in a selected patient population using a particular device in a procedure performed by a specific pool of physicians at specific facilities. While these trials provide invaluable efficacy information, they are expensive to conduct and do not necessarily provide the full gamut of information needed.

STS and ACC: Two Professional Societies with Extensive Experience and Expertise in Clinical Registries

ACC and NCDR

Existing clinical data repositories can be leveraged to evaluate patient selection, procedure indications, peri-procedural outcomes and longitudinal safety surveillance and patient outcomes. ACC's National Cardiovascular Data Registry® (NCDR) is one example of such an existing clinical data infrastructure. In 1997 the ACC launched the NCDR as a result of its exploration of various strategies for collecting and implementing clinical data to improve cardiovascular care. The outgrowth of that effort focused on quality patient care through standardized measurement of clinical practice and patient outcomes. Then, as now, NCDR is committed to including clinicians and care providers in its leadership and to using standardized, clinically relevant data elements and scientifically appropriate methods to collect, analyze and report clinical outcomes.

⁶ Biner S, Perk G, Kar S, Rafique AM et al. Utility of Combined Two-Dimensional and Three-Dimensional Transesophageal Imaging for Catheter-Based Mitral Valve Clip Repair of Mitral Regurgitation. J Am Soc Echocardiogr 2011;24:611-617.

Today, more than 2,200 hospitals nationwide participate in the NCDR. As the US' preeminent cardiovascular data repository, the NCDR provides evidence-based quality improvement solutions for cardiologists and other medical professionals who are committed to measurement, improvement and excellence in cardiovascular care. A trusted, patient-centered resource, the NCDR has developed clinical modules, programs and information solutions that support the areas of cardiovascular care where quality can be measured, benchmarked and improved to make a difference in patients' lives.

NCDR data has been studied for a variety of purposes, including consistency with guidelines,⁷ appropriateness,⁸ and comparative effectiveness, to name a few.⁹ The FDA has long been a supporter of NCDR, providing funding for the Improving Pediatric and Adult Congenital Treatment (IMPACT) Registry and development of a possible atrial fibrillation registry. NCDR is also a participant in the FDA's Sentinel Initiative, looking at methods of drawing on registry data as a mechanism of providing safety signals to the FDA. ACC recently completed work comparing the effectiveness of revascularization strategies by linking NCDR and STS' clinical database with administrative databases, including the Social Security Death Master File and the Centers for Medicare and Medicaid Services (CMS) Provider and Analysis Review data. We look forward to continuing to work collaboratively on these initiatives.

STS National Database

The STS National Database was established in 1989 as an initiative for quality improvement and patient safety among cardiothoracic surgeons. There are three components to the STS National Database, each focusing on a different area of cardiothoracic surgery—Adult Cardiac, General Thoracic, and Congenital Heart Surgery, with the availability of Anesthesiology participation within the Congenital Heart Surgery Database. The Database has grown exponentially over the years, both in terms of participation and stature.

The component Databases provide opportunities for quality improvement to their participants. The Society has developed quality performance measures in all three sub-specialties of surgery, and these measures have either been endorsed or are in the process of being considered for endorsement by the National Quality Forum. By collecting outcomes data for submission to the STS National Database, surgeons are committing to improving the quality of care that their cardiothoracic surgery patients receive. The Database has demonstrated the ability to be a powerful tool for clinical research. Since its inception, more than 100 publications have been derived from Database outcomes. These studies have been published in a variety of professional journals and textbooks and have significantly advanced knowledge in cardiothoracic surgery. The Database continues to expand with new initiatives. Launched in January 2011, STS Public Reporting Online enables Database participants to voluntarily report to the public their heart bypass surgery performance. Overall composite star ratings as well as their component ratings are listed on sts.org for more than 250 Database participants. The Adult Cardiac Surgery Database, now containing more than 4.5 million surgical records, represents approximately 95 percent of all adult cardiac surgery centers across the U.S. With the success of participation nationally, STS launched in 2011

⁷ Chan PS, Patel MR, Klein LW, et al. Appropriateness of Percutaneous Coronary Intervention. JAMA 2011; 306(1):53-61.

⁸ Al-Khatib SM, Hellcamp A, Curtis J, et al. Non-evidence-based ICD implantations in the United States. JAMA 2011; 305(1):43-49.

⁹ Funded by a National Heart, Lung, and Blood Institute American Recovery and Reinvestment Act Grant, the ASCERT Study represents a unique collaboration between the ACCF and STS to study the comparative effectiveness of percutaneous coronary intervention and coronary artery bypass graft surgery in patients with stable coronary artery disease.

an initiative to accommodate Database participation worldwide by including international participants in the Adult Cardiac Surgery Database.

The STS-ACC TVT Registry

To learn more about transcatheter valve therapies, the ACC and STS worked together to create the Transcatheter Valve Therapy (TVT) Registry™. It launched in December 2011 as a method for monitoring the safety and efficacy of the new TAVR procedure for the treatment of aortic stenosis with the intention of expanding the Registry to include other transcatheter-based therapies for the treatment of structural heart disease. Through the capture and reporting of patient demographics, procedure details, and facility and physician information, the TVT Registry provides a data repository capable of delivering insight into clinical practice patterns and patient outcomes. To date, 196 sites have enrolled in the TVT Registry, with that number increasing as more sites and operators are trained on the device and procedure. The TVT Registry is the vehicle for one of the FDA-mandated post approval studies for the Edwards Sapien Transcatheter Heart Valve for its original approved indications, the transfemoral approach in patients who are determined not to be surgical candidates. The FDA has also approved the use of the TVT Registry to conduct an investigational device exemption (IDE) study (G120291. ClinicalTrials.gov Identifier: NCT01787084) using the Edwards Sapien Transcatheter Heart Valve for procedures involving alternative methods of accessing the aortic valve. Additionally, as of May 1, 2012, the Centers for Medicare and Medicaid Services (CMS) mandates participation in a national study for coverage of the TAVR procedure.¹⁰ The ACC/STS TVT Registry continues to be the only study that meets the criteria set forth in the CMS National Coverage Decision (NCD).

There are certain efficiencies to be gained from using registries such as the TVT Registry for post-market research and surveillance. It increases the collaboration between industry and the professional societies, providing an increased level of credibility to the data and findings. The TVT Registry has the ability to conduct site recruitment, patient randomization and data audits. Additionally, because of the existing registry structure, there are a large number of pre-defined data elements and procedures already available as NCDR and the STS Database expand. That said, additional data fields can be added as necessary, as we have done to accommodate the TVT Registry. This can be easily seen from the attached data collection tool for the TVT Registry.

The TVT Registry is governed by a joint Steering Committee with representatives from the STS and ACC selected through each society's standard selection process. Given the importance and broad function of the registry, it is important that representatives have current relevant clinical background and expertise with large data registries – and be recognized as leaders in their field. The Steering Committee also includes representation from the FDA, CMS, the National Heart Lung and Blood Institute and the Duke Cardiovascular Research Institute. The TVT Registry Research and Publications Subcommittee and Stakeholder Advisory Group allow for input from multiple stakeholders, including industry trial sponsors, consumers, researchers, and health plans so that the registry benefits from the wisdom of many constituencies

There are many benefits to using a clinical registry for post-market surveillance, and specifically, to using the TVT Registry for post approval studies, ongoing IDE studies, and other forms of research. They are:

- **Ability to focus on previously identified critical issues.** The TVT Registry has been designed to clarify certain risks that have been identified as key issues based on reviews of the initial clinical data.

¹⁰ [http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?&NcaName=Transcatheter%20Aortic%20Valve%20Replacement%20\(TAVR\)&bc=AiAAAAAIAAA&NCAId=257&](http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?&NcaName=Transcatheter%20Aortic%20Valve%20Replacement%20(TAVR)&bc=AiAAAAAIAAA&NCAId=257&)

- **Development of risk models tailored for the TVT population.** Models of outcomes will be developed and validated using TVT Registry data that can provide personalized risk estimates.
- **Tracking of long-term and quality of life outcomes.** The TVT Registry is linked to CMS claims data to evaluate longitudinal patient outcomes, including hospitalizations, survival, and quality of life measures.
- **Decision-making tools for patients, families, clinicians and regulators.** From registry data, we will be able to furnish clinicians, patients, and families with data and tools to make informed decisions about the different treatment options.
- **Appropriateness of Care.** Data collected over years can be analyzed for the appropriateness of the procedure by correlating patient characteristics with post-procedural outcomes.
- **Potential Expansion of Indications for Use.** The TVT registry will gather data on device use in ways not originally intended, enabling us to understand more about the real world implications of new devices. Recently an IDE study has been approved by the FDA and CMS that is sponsored by the STS and ACC. This research study will investigate the use of alternative access routes for TAVR in inoperable patients. This IDE study demonstrates how professional societies, working with the FDA and CMS, are driving regulatory improvements and novel approaches to studying new technologies, as well as potentially expanding patient access with independently designed, conducted, and analyzed studies to develop the evidence needed to consider expanded indications. The TVT Registry is the infrastructure used for this, and several additional IDE studies are currently being designed.

The TVT Registry was conceived to address these issues of central importance, so as to better define and refine the use of transcatheter valve therapies in patients with structural heart disease. It also was designed to accommodate both the expansion of the indications for previously FDA approved technologies as well as newly approved technologies. The ACC and STS intend to expand this data set to include elements relevant to mitral valve repair. Preliminary discussions with Abbott Vascular have already occurred regarding their interest in utilizing the TVT Registry.

While the current application is only for inoperable patients, it is not difficult to envision a day when the MitraClip or other similar transcatheter mitral valve therapy might be an option for patients who are considered acceptable surgical candidates. As such, future clinicians, patients, and their families in the US will need to make informed decisions choosing between these two treatment strategies. This will reinforce the need for a multidisciplinary heart team, and the ACC-STS partnership will serve as such a partnership on a national level. These choices in different approaches to valve replacement will also amplify the need for gathering data to understand how such treatment decisions are made and the consequent outcomes. The STS-ACC TVT Registry gathers patient reported outcomes, including longitudinal quality of life measures, and has the flexibility to gather additional data to capture the drivers of the clinician's and patient's preferences for treatment. Patients and their families will need to make informed decisions regarding the likelihood of having a mortality benefit, of improving their functional class and quality of life, of suffering a complication, and of choosing between different care options and therapeutic approaches. As outlined in the vision of the Patient Centered Outcomes Research Institute, informed health care decisions must be based on high-integrity, evidence-based information that is patient-centric. ACC and STS share this vision, and as such, a major goal of the TVT Registry is the collection, analysis, and practical application of knowledge gained through the experience of thousands of patients undergoing these novel therapies in real-world practice.

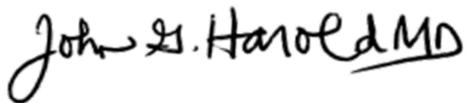
Conclusion

ACC and STS recognize the excitement in the cardiovascular community of the potential availability of new less-invasive technology to a wider spectrum of patients, and we applaud the efforts of those seeking

to bring this new procedure to the US. We understand the need to ensure only the highest quality patient care is provided, especially to the inoperable patient population at issue today. The ACC and STS are pleased to see that the excitement over the new technology is tempered by efforts to ensure responsible dissemination of it. We are working hard to align our efforts with our fellow specialty societies – ASE, HFSA, SCAI, and the American Association for Thoracic Surgery – as a way of doing our part to ensure that the physician community is prepared to provide high quality care using the newest technology and techniques to patients with cardiovascular disease. The STS and ACC appreciate the efforts of the FDA to date and looks forward to continuing to work with the Agency to protect the interests of cardiovascular patients.

The STS and ACC appreciate the opportunity to provide the FDA’s Advisory Panel on Circulatory System Devices with input pertaining to application for approval for use of Abbott Vascular’s MitraClip System and would welcome the opportunity to discuss this input further. We look forward to working with the FDA on this and future issues. Please direct any questions or concerns to the STS Director of Government Relations Phil Bongiorno at (202) 787-1221 or pbongiorno@sts.org or Lisa P. Goldstein, JD, ACC Associate Director for Regulatory Affairs at (202) 375-6527 or lgoldstein@acc.org.

Sincerely,



John Gordon Harold, MD, MACC, MACP, FESC, FCCP, FAHA
President
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Douglas E. Wood, MD
President
The Society of Thoracic Surgeons