Summary of Safety and Effectiveness Data (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Endovascular Graft
Device Trade Name:	Talent™ Thoracic Stent Graft System
Applicant Name and Address:	Medtronic Vascular 3576 Unocal Place Santa Rosa, CA 95403 USA
Premarket Approval Application (PMA) Number:	P070007
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	June 5, 2008
Expedited:	Not Applicable

II. INDICATION FOR USE

The Talent™ Thoracic Stent Graft System is intended for the endovascular repair of fusiform aneurysms and saccular aneurysms/penetrating ulcers of the descending thoracic aorta in patients having appropriate anatomy, including:

- Iliac/femoral access vessel morphology that is compatible with vascular access techniques, devices, and/or accessories;
- Non-aneurysmal aortic diameter in the range of 18 – 42mm; and
- Non-aneurysmal aortic proximal and distal neck lengths ≥ 20mm.

III. CONTRAINDICATIONS

The Talent™ Thoracic Stent Graft is contraindicated in:

- Patients who have a condition that threatens to infect the graft.
- Patients with sensitivities or allergies to the device materials.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Talent™ Thoracic Stent Graft System labeling (Instructions for Use).

V. DEVICE DESCRIPTION

Talent™ Thoracic Stent Graft System

The Talent™ Thoracic Stent Graft is pre-loaded into the CoilTrac Delivery System. The loaded delivery system is inserted endoluminally via the femoral or iliac artery and tracked through the patient's vasculature to deliver the stent graft to the target site.

Talent™ Thoracic Stent Graft

The Talent™ Thoracic Stent Graft is composed of a series of shaped, self-expanding nitinol springs to form a stent. The self-expanding nitinol stent is covered by a polyester woven graft. The graft material is sewn to the stent. Radiopaque markers are sewn to the graft to help visualize and identify the edge of the graft material, stent graft alignment, and the minimum overlap required when multiple stent grafts are used.

The Talent™ Thoracic Stent Graft System is a modular device system that accommodates the use of multiple stent graft sections. Depending on the patient's anatomy, single or multiple stent grafts may be required to achieve coverage and exclude the target lesion. The Talent™ Thoracic Stent Graft offers multiple graft configurations in order to support optimum matching of the device(s) to individual patient anatomies. Different proximal and distal end configurations accommodate patient anatomy and allow graft mating. Figure 1 illustrates the various stent graft end configurations, and Table 1 summarizes the features of various modular stent graft component sections.

Figure 1: Talent™ Thoracic Stent Graft End Configurations

FREE FLO BARE SPRING OPEN WEB CLOSED WEB

Table 1: Talent™ Thoracic Stent Graft Component Summary

Component	Proximal End Configuration	Distal End Configuration	Total Length	Covered Length	Available Diameters	Straight or Tapered Tube
Proximal Main Section	FreeFlo (>22mm) Bare Spring (22mm)	Closed Web	130mm	112-116mm	22mm – 46mm	Straight Tube
Distal Main Section	Open Web	Closed Web	130mm	110-114mm	26mm – 46mm	Tapered Tube
Proximal Extension	FreeFlo	Open Web	80-90mm	46-54mm	26mm – 46mm	Straight Tube
Distal Extension	Open Web	Bare Spring	80-90mm	46-54mm	26mm – 46mm	Straight Tube

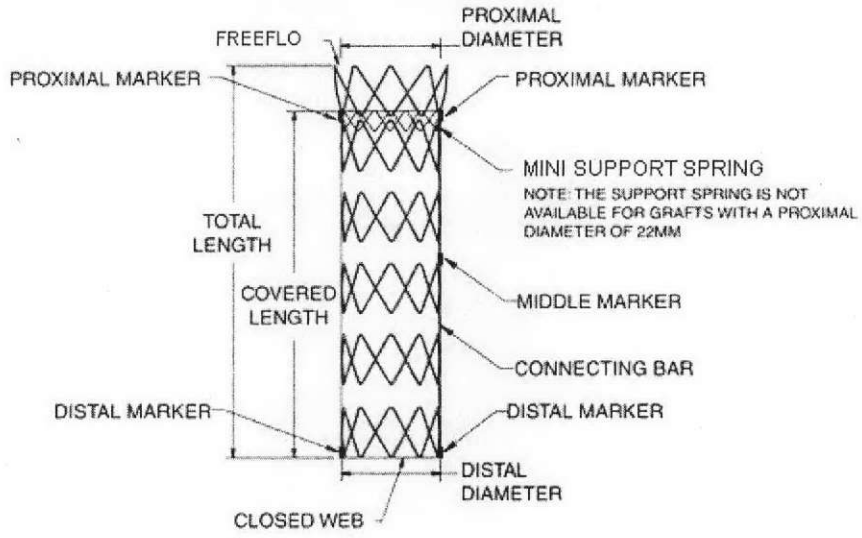
Selection of Stent Grafts

Stent graft sizing, component selection, required overlap between components, and order of component deployment is provided in the Instructions for Use (IFU).

Proximal Main Section

The proximal main section has an uncovered nitinol spring as the proximal end configuration, which allows for trans-vessel flow. Proximal main stent grafts with a proximal diameter greater than 22mm have a mini-support spring to aid in sealing. The proximal end configuration in which an uncovered nitinol spring and mini-support spring are present is called the 'FreeFlo' configuration. The proximal end configuration in which an uncovered nitinol spring is present without a mini-support spring is called a 'Bare Spring' configuration. The distal end of the stent graft has a closed web configuration.

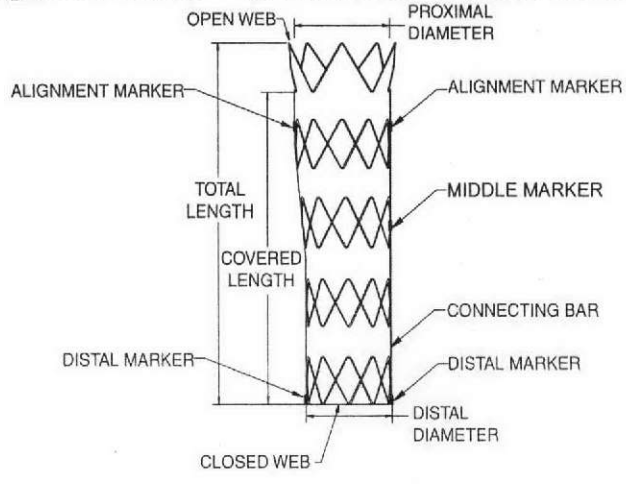
Figure 2: Talent™ Thoracic Main Section



Distal Main Section

Distal main sections are typically used to increase the length of coverage of the treated vessel when the proximal main section is inadequate in length to exclude the aneurysm. The distal main section utilizes a proximal configuration in which the outline of the most proximal spring is covered with fabric leaving a "tulip" effect, called open web. The distal configuration is a closed web configuration.

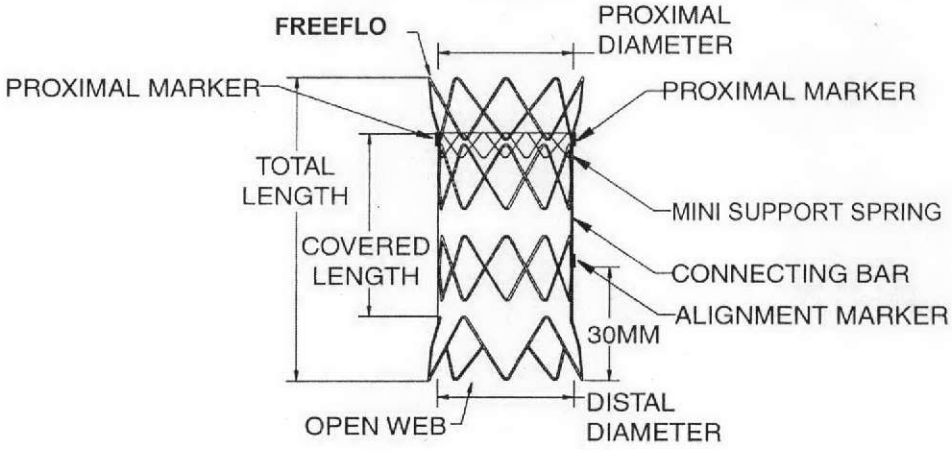
Figure 3: Talent™ Thoracic Distal Main Section



Proximal Extension

Proximal extensions are intended to be used when the proximal end of a previously implanted stent graft requires extension to fully exclude the target lesion, or to treat proximal Type I endoleaks. The proximal extension is deployed within the proximal end of the previously implanted stent graft. The proximal end of the stent graft has a FreeFlo configuration, which allows for trans-vessel flow. The distal end of the stent graft has an open web configuration.

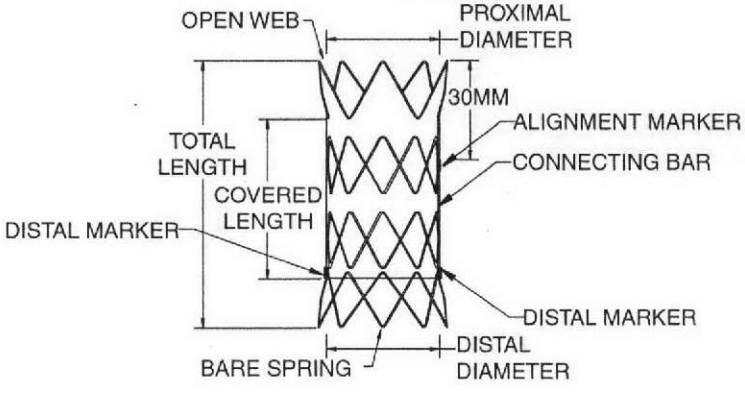
Figure 4: Talent™ Thoracic Proximal Extension



Distal Extension

Distal extensions are intended to be used when the distal end of a previously implanted stent graft requires extension to fully exclude the target lesion, or to treat distal Type I endoleaks. The distal extension is deployed in the distal end of the previously implanted stent graft and extends distally. The proximal end has an open web configuration. The distal configuration has a bare spring extending beyond the edge of the fabric, which allows for trans-vessel flow.

Figure 5: Talent™ Thoracic Distal Extension

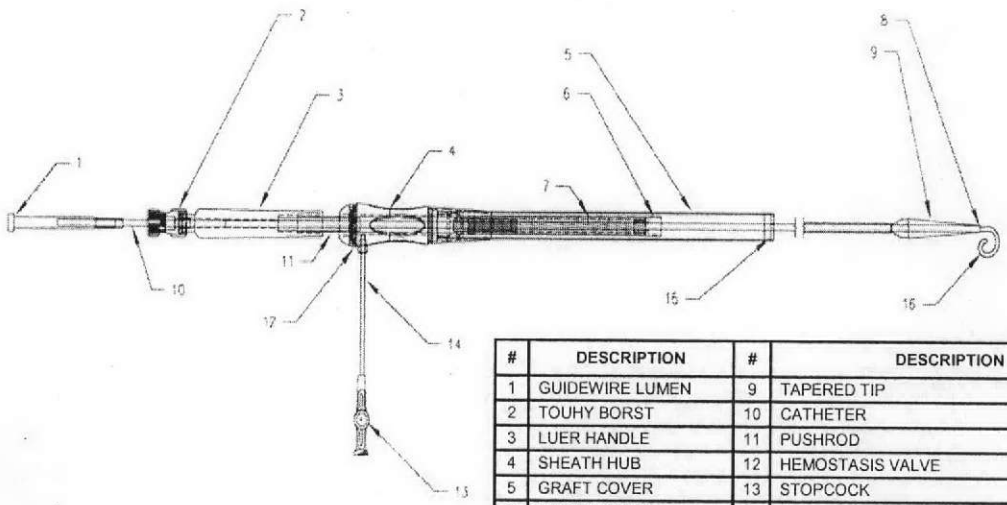


CoilTrac Delivery System

The CoilTrac Thoracic Delivery System is composed of an inner catheter with a tapered tip, a push rod shaft with spring and cup plunger, and a graft cover. The inner catheter allows tracking of the system over a 0.035" guidewire, the push rod shaft with spring and cup plunger is the deployment platform, and the graft cover is for graft containment and deployment. The

nose of the system is a flexible tapered tip. The graft cover has a hemostasis valve at the proximal section and a radiopaque marker band at the distal end. The radiopaque marker indicates the edge of the sheath under fluoroscopy. The crossing profile of the delivery catheter is 22, 24, or 25Fr, depending upon the size of the stent graft chosen. See Figure 6.

Figure 6: CoilTracDelivery System



#	DESCRIPTION	#	DESCRIPTION
1	GUIDEWIRE LUMEN	9	TAPERED TIP
2	TOUHY BORST	10	CATHETER
3	LUER HANDLE	11	PUSHROD
4	SHEATH HUB	12	HEMOSTASIS VALVE
5	GRAFT COVER	13	STOPCOCK
6	CUP PLUNGER	14	SIDE PORT EXTENSION
7	PUSHROD SPING COIL	15	RADIOPAQUE MARKER
8	DISTAL PORT	16	TRANSPORT WIRE (REMOVE BEFORE USE)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of thoracic aortic aneurysms (TAA): endovascular repair using another endovascular grafting system; surgical implantation of a synthetic graft within the aneurysmal vessel; and medical management. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

Currently, the Talent™ Thoracic Stent Graft System is available in over 50 regions, including: the European Union; Asia; Africa; the Middle East; Latin America; Australia; and New Zealand. The device has not been withdrawn from the market for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects (e.g., complications) that may occur and/or require intervention with the use of this device include, but are not limited to:

- Amputation
- Aneurysm Enlargement
- Balloon rupture
- Breakage of the metal portion of the device
- Cardiac Failure/Infarction
- Change in mental status
- Conversion to open surgery
- Death
- Deployment difficulties
- Edema
- Embolization
- Endoleak
- Erectile Dysfunction
- Erosion with fistula or pseudoaneurysm
- Failure to deploy
- Gastrointestinal complications, including: adynamic ileus, bowel (ileus, transient ischemic, infarction, necrosis)
- Graft twisting and/or kinking
- Hemorrhage/Bleeding
- Inaccurate placement
- Infection and fever
- Insertion and removal difficulties
- Intercostal pain
- Neurological complications, including: spinal cord ischemia with paraplegia; paraparesis and/or paresthesia; Cerebral Vascular Accidents (CVA); Transient Ischemic Attacks (TIA); neuropathy; and blindness
- Prosthetic thrombosis
- Pulmonary complications
- Renal failure
- Rupture of graft material
- Ruptured vessel/aneurysm sac enlargement
- Stent graft migration
- Vascular complications, including: thrombosis; thromboembolism; occlusion (arterial and venous); vessel dissection[1] or perforation; collateral vessel occlusion; vascular ischemia; tissue necrosis; and amputation
- Wound healing complications.

For the specific adverse events that occurred in the clinical studies, see Section X below.

[1] Aortic dissection is an infrequent but recognized risk of endovascular repair. In the first 10 years of clinical experience (outside the U.S. (OUS) - commercial and U.S. - investigational), there were 39 reported events of retrograde dissection in patients. Of the 39 reported events, 33 patients had a pre-existing aortic dissection

IX. SUMMARY OF PRECLINICAL STUDIES

A. Biocompatibility

Toxicology and biocompatibility testing was conducted for materials in the Talent™ Thoracic Stent Graft System. Testing was conducted in accordance with Good Laboratory Practices (21 CFR §58) and ANSI/AAMI/ISO 10993-1: 2003 *Biological Evaluation of Medical Devices.* The Talent™ Thoracic Stent Graft was classified per ISO 10993-1 *Biological Evaluation of Medical Devices* as an implant device in permanent contact (> 30 days) with blood. The CoilTrac (Thoracic) Delivery System was classified as an externally communicating device in limited contact (< 24 hours) with circulating blood.

Table 2 summarizes the test results for the Talent™ Thoracic Stent Graft. Table 3 summarizes the test results for the CoilTrac (Thoracic) Delivery System. All the results of the toxicology and biocompatibility testing were acceptable.

Table 2: Summary of Biocompatibility Testing – Talent™ Thoracic Stent Graft

Test Name	Purpose	Results	Pass/Fail
Cytotoxicity: Colony Assay	Evaluate effect of leaching substances on colony formation (Chinese Hamster Lung Cell)	Average colony formation (% of controls): 91-109%	Pass
MHLW Maximization Sensitization	Determine test article potential to cause delayed dermal sensitization (Guinea Pig)	1%, 10% and 100% test article extracts showed no evidence of causing sensitization. All test animals were graded 0	Pass
ISO Irritation/ Intracutaneous Toxicity	Determine local dermal irritant effects of leachables extracted from the test article (Rabbit)	Difference between test and control scores: Saline: 0.0 Sesame Oil: 0.0	Pass
MHLW Systemic Toxicity	Determine potential of leachables extracted from the test article to cause acute systemic toxicity (Mouse (strain Crl:CF-1BR))	No evidence of mortality or systemic toxicity	Pass
4-wk Sub-Chronic Toxicity (Subcutaneous Implantation)	Evaluate potential sub-chronic toxicity (Rat)	No evidence of systemic toxicity Local Macroscopic tissue reaction not significant compared to the negative control Microscopically considered a slight irritant	Acceptable
Genotoxicity: Bacterial Reverse Mutation Study (AMES)	Determine whether extract causes mutagenic changes in the test strains in the presence or absence of S9 metabolic activation (*Salmonella typhinurium* strains TA98, TA 100, TA1535, and TA1537; *Esherichia coli* strain WP2*uvr*A)	No case of ≥ 2-fold increase in mean # of revertants	Pass

Test Name	Purpose	Results	Pass/Fail
Genotoxicity: *in vitro* Chromosomal Aberration	Determine whether the test extract causes genotoxicity in the presence and absence of S9 metabolic activation. (Chinese Hamster Ovary cells)	Test extracts were concluded to be negative for the induction of structural chromosome aberrations in Chinese Hamster Ovary Cells: χ^2= 0.5 and 1.2	Pass
Genotoxicity: Mouse Peripheral Blood Micronucleus	Evaluate test extract potential to cause genotoxic changes in the chromosomes or the mitotic apparatus of murine polychromatic erythrocytes (Mouse (strain Crl:CD-1(ICR) BR))	No statistically significant increase in the # of MN-RETs for each test group	Pass
12 week ISO Muscle Implantation	Evaluate evidence of irritation or toxicity, post-implantation (Rabbit)	Macroscopic Score: 0.0 = 'Not Significant' Microscopic Score: 4.4 ='Slight Irritant'	Acceptable
Hemocompatibility: MHLW *in vitro* Hemolysis	Evaluate if test article extract causes hemolysis (Rabbit)	• 1 hr & 2 hrs: 0% • 4 hrs: 1.1%	Pass
C3a Complement Activation Assay	Ensure that the potential extractables did not activate the complement system (Extract: Normal Human Serum (NHS))	C3a concentration not significantly higher than the controls	Pass
Partial Thromboplastin Time Assay	Detect material mediated effects on the intrinsic coagulation pathway (Extract: Human Citrated Plasma)	Shortened clotting time compared to negative control	Acceptable
in vivo Thromboresistance	Evaluate the potential of the test device to resist thrombus formation when placed in the vasculature (Dog)	Grade 1, 2 & 2. Test article was thromboresistant. (Note: Test Article = finished device)	Pass
USP Pyrogen Study	Determine if the test solution induced a pyrogenic response (Rabbit)	Initial test: 1 rabbit was 0.6° above baseline temperature Retest: 1 rabbit of the 8 total had an increase of 0.5°C or above. Total rise for all 8 rabbits was 1.3°C	Pass

Table 3: Summary of Biocompatibility Testing – Talent™ Thoracic CoilTrac Delivery System

Test Name	Purpose	Results	Pass/Fail
Cytotoxicity: Colony Assay	Evaluate effect of leaching substances on colony formation (Chinese Hamster Lung Cell)	Average colony formation (% of controls): 91-110%	Pass
MHLW Maximization Sensitization	Determine test article potential to cause delayed dermal sensitization (Guinea Pig)	0.1%, 1% and 10% Test Article Extracts showed no evidence of causing sensitization. All Test Animals were graded 0	Pass
ISO Irritation/ Intracutaneous Toxicity	Determine local dermal irritant effects of leachables extracted from the test article (Rabbit)	Difference between test and control scores: Saline: 0.0 Sesame Oil: 0.0	Pass
MHLW Systemic Toxicity	Determine potential of leachables extracted from the test article to cause acute systemic toxicity (Mouse (strain Crl: CF-1 BR))	No evidence of mortality or systemic toxicity	Pass
Hemocompatibility: MHLW *in vitro* Hemolysis	Evaluate if test article extract causes hemolysis (Rabbit)	• 1 hr & 2 hrs = 0% • 4 hrs = 1.3%	Pass
C3a Complement Activation Assay	Ensure that the potential extractables did not activate the complement system (Extract: Normal Human Serum (NHS))	C3a concentration not significantly higher than the negative control	Pass
Partial Thromboplastin Time Assay	Detect material mediated effects on the intrinsic coagulation pathway (Extract: Human Citrated Plasma)	Shortened clotting time compared to negative control.	Acceptable
In vivo Thromboresistance	Evaluate the potential of the test device to resist thrombus formation when placed in the vasculature (Dog)	Grade 1, 2 & 2. Test article was thromboresistant. (Note: Test Article = finished device)	Pass
USP Pyrogen Study	Determine if the test solution induced a pyrogenic response (Rabbit)	All animals < 0.5° C increase.	Pass

B. Product Testing

Medtronic conducted comprehensive pre-clinical, bench and analytical testing on the Talent™ Thoracic Stent Graft System. The *in vitro* testing was intended to verify that the performance attributes of the Talent™ Thoracic Stent Graft System are sufficient to minimize adverse events under anticipated clinical conditions. This testing included both the stent graft and the delivery system. All testing was conducted in accordance with national and international standards and guidance documents.

The testing detailed in Table 4 verified that the Talent™ Thoracic Stent Graft System (implant and delivery system) met its product performance and design specifications. Results obtained from *in vitro* testing provided evidence supporting the safety and effectiveness of the Talent™ Thoracic Stent Graft System.

Table 4: Summary of Testing of Talent™ Thoracic Stent Graft System

Test	Specification / Acceptance Criteria	Summary Test Results
Stent Graft Visual Integrity	• No broken stents • 5-13 sutures/cm density (springs) • Loose sutures are allowable if they continue to attach the stent and/or RO marker to the graft material. • No graft holes or tears • Support springs may contain deformation if the spring remains attached to the graft material	All samples met the acceptance criteria.
Spring Radial Force	Characterization study	The mean forces were found to be 1.38 lbf, 1.48 lbf and 1.12 lbf for the 32mm, 40mm and 46mm springs respectively. This testing demonstrates the ability of the Talent™ Stent Graft to exert an outwardly positive radial force on the graft, allowing the Talent™ Stent Grafts to expand and maintain an open lumen and provide sealing in a variety of patient anatomies.
Stent Graft Dimensional Verification	Diameter ≥ nominal diameter - 1 mm	All samples met the acceptance criteria.
Stent Graft Conformability	The stent graft kink radius must accommodate a 90° bend without kinking	All samples met the acceptance criteria.
Stent Graft Migration Resistance	Characterization study	This testing characterizes the proximal pullout force of the main device following deployment in a mock aorta. The mean peak force required to displace the proximal section of the stent graft was 1228.18 gf. Based upon these results, component migration appears unlikely.
Stent Graft Joint Strength	Characterization study	This testing characterizes the ability of the modular components of the Talent™ Stent Graft System to resist separation. The mean peak force required to displace a Distal Main section from a Proximal Main section was 190.54 gf.
Spring Attachment Strength	Characterization study	This testing quantified the attachment strength of the Talent™ Stent Graft springs to the graft material. The strength ranged from 22.98 to 44.86 lbf for bare springs and from 52.13 to 89.69 lbf for body springs.
Crimp Strength	Crimp strength must be greater than 5.25 lbf for 32mm, 6.03 lbf for 40mm and 6.05 lbf for 46mm.	All samples met the acceptance criteria.

Test	Specification / Acceptance Criteria	Summary Test Results
Nitinol Alloy Material and Surface Analysis	**Property-Requirement** Chemical Composition Nickel: 55.9% reference Titanium: Balance Carbon: <0.05% Oxygen: <0.05% Any single trace element: <0.05% Total trace elements (Other than Ni, Ti, C, and O): <0.4% Transformation Property A_s temperature: -15 +/- 5°C Mechanical Properties UTS (ksi): 206 – 246 ksi Elongation (%): 4% min	All samples met the acceptance criteria.
Surface Analysis	Must be smooth and uniform in color with no blotches, spotting or pinholes	All samples met the acceptance criteria.
Potentiodynamic Polarization Corrosion	Characterization Test	This testing evaluated, per ASTM F2129, the general resistance of springs to pitting in the simulated clinical conditions. The test results indicate that the stent springs used in the Talent™ Thoracic Stent Grafts have a high resistance to localized corrosion under simulated in-vivo conditions.
MRI	The presence of the stent graft must not pose an additional unacceptable risk to patients when subjected to 1.5T and 3.0T magnetic fields.	All samples met the acceptance criteria. The device has therefore been determined to be MRI-conditional.
Graft Component Tensile Strength	Characterization study	Graft component tensile strength testing was conducted to characterize the tensile strength of the graft material. The mean tensile strength of material was 55.19 lbf.
Stent Graft Permeability	Characterization study	This testing characterizes the rate of water flow through the Talent™ Thoracic Stent Graft under a pressure of 120 mm Hg. The mean rate of leakage per unit area was calculated as 487.17 ml/min/cm^2. The water permeability observed is consistent with the water permeability of polyester materials used in endovascular and vascular applications.
Stent Graft Burst	Stent graft burst pressure LTL ≥ 18.8 psi	All samples met the acceptance criteria.

Test	Specification / Acceptance Criteria	Summary Test Results
Finite Element Analysis	Characterization study	Finite element analysis was used to determine the location and magnitude of the maximum strains in the Nitinol wire frame as a function of radial compression when subjected to catheter loading and an *in vivo* pulsatile loading environment. The peak strains at simulated catheter loading were determined to be below the yield strain of the Nitinol springs. Maximum strain locations and values determined from the simulated *in vivo* pulsatile loading were subsequently used as a reference in appropriate *in vitro* testing including pulsatile fatigue testing.
Whole Spring Fatigue	No fractures over 400 million cycles of clinically relevant loading conditions.	All samples met the acceptance criteria.
Graft Material and Seam Fatigue Testing	No unacceptable (based on individual sample evaluation) seam damage, suture propagation, or suture-hole elongation over 400 million cycles of clinically relevant loading conditions.	All samples met the acceptance criteria.
Whole Device Fatigue Testing	Must demonstrate structural integrity over 400 million cycles. No structural failures of the device that would compromise spring to graft attachment or patency. No graft material failure as a result of interaction of stent-graft components with each other.	All samples met the acceptance criteria.
Delivery Catheter Tensile Bond Strength Tests	Varies depending upon specific test. Acceptance criteria ranged from 5.0 lbf to 35 lbf.	All samples met the acceptance criteria.
Delivery Catheter Torsional Bond Strength Tests	Ultimate Torsional Strength > 1.62 lb•in	All samples met the acceptance criteria.
Sheath Marker Visualization	Characterization study	The radiopacity of the introducer sheath (graft cover) radiopaque marker was evaluated in ovine models under fluoroscopy.
Graft Cover Tensile Strength	Yield Strength LTL > Deployment Force UTL	All samples met the acceptance criteria.
Delivery System Hemostasis	Water leakage flow rate < 2 ml/min	All samples met the acceptance criteria.

Test	Specification / Acceptance Criteria	Summary Test Results
Trackability / Pushability	Characterization study	Trackability/pushability testing was conducted to characterize the force required to track the delivery system over a guidewire through a tortuous path. The mean force required for pushability and trackability of the delivery systems under worse case scenarios (largest diameter and longest length stent grafts) ranged from 1260.90 gf to 1906.47 gf.
Guidewire Acceptance	Delivery system must pass 0.035" diameter guidewire with minimal resistance and without damaging the delivery system or guidewire.	All samples met the acceptance criteria
Deployment Force	Deployment Force UTL must be less than Sheath to Hub Bond Strength LTL and Graft Cover Yield Strength LTL	All samples met the acceptance criteria
Delivery System Torquability	Characterization study	Delivery system torquability testing was conducted to characterize the torque (rotational) response of the stent graft system within simulated vasculature.
Delivery System Kink Radius	Characterization study	Delivery system kink radius testing was conducted to characterize the delivery system kink radius by determining the minimum radius of curvature to forcefully produce a kink. For the worst case (largest diameter stent with largest diameter delivery system) the mean radius to create a kink was observed to be 10.25cm.
Crossing Profile	The maximum outer diameter must be less than 1 Fr size over the nominal size.	All samples met the acceptance criteria
Working Length	Working length must be 90 ± 1cm	All samples met the acceptance criteria

C. Animal Studies

Three primary animal studies were conducted in the development of the Talent™ Thoracic Stent Graft System. One study was performed in a canine model and two in a swine model. All devices were of dimensions consistent with human clinical use. Two studies [swine (n=15) and canine (n=5)] evaluated smaller diameter devices implanted in the infra-renal aorta. The third study [(swine (n=5)] evaluated large diameter devices implanted in the thoracic aorta. Based on the results of the pre-clinical testing presented in this model, the Talent™ Thoracic Stent Graft System is capable of being successfully delivered and deployed in the animal aorta, maintaining integrity and vessel patency, and does not instigate unacceptable mechanical damage or immune response to the vessel. These studies are summarized in the Table 6 below.

Table 5. Summary of non-clinical *in vivo* studies

Study	Animal Model	Purpose	Results and Interpretation
Talent™ Stent Study	Porcine (15 animals)	Stent Graft System ability to be placed in a living animal aorta and the ability of the implant to maintain patency and apposition to the vessel wall	Technical Success (15 animals) Successful implants at the target location. Device Associated Events: Integrity, Patency Migration (7 animals) Springs and graft material intact, maintained integrity. Patent lumens with no evidence of thrombus in stent graft. Histopathology (7 animals) Device well tolerated (63 days – 251 days), as evidenced by patent lumen and lack of significant chronic inflammatory response. Neo-intimal formation in process.
A Safety and Efficacy Study Evaluating the World Medical Endoluminal Stent-graft in the Thoracic Aorta of Swine	Porcine (5 animals)	Acute and chronic performance and biocompatibility 12-weeks in a porcine vascular model. Histological analysis	Technical Success (5 animals) Deployment: Successful implants at the target location. Device Associated Events: Integrity, Patency Migration (4 animals) Devices maintained integrity with no evidence of spring or graft material failure. Patent lumens with no evidence of significant occlusions. Excellent proximal and distal device fixation with native vessel wall, with no evidence of migration. Appropriate aortic blood flow. Histopathology (4 animals) Gross pathology normal and similar to adjacent tissue. Lack of significant inflammatory response. Cellular infiltration into luminal surface for neo-intimal formation. Tissue growth consistent with healing response leading to formation of a stable neo-intimal lining.
Pre-Clinical Study Evaluating the World Medical Endoluminal Stent Graft in a Canine Model	Canine (5 animals)	Acute and chronic performance and biocompatibility at 12 weeks in a canine vascular model. Histological analysis was also performed	Technical Success (5 animals) Deployment: successfully at the target location for all five (5) animals. Device Associated Events: Integrity, Patency Migration. (5 animals) Devices maintained integrity with no evidence of spring or graft material failure. Grafts widely patent at the time of removal. Histopathology (5 animals) All animals tolerated the implant procedures well. Gross pathology normal and similar to adjacent tissue. Lack of significant inflammatory response. Cellular infiltration into luminal surface for neo-intimal formation. Tissue growth consistent with normal healing response leading to formation of a stable neo-intimal lining.

D. Packaging, Shelf Life Testing, and Sterilization

The Talent™ Thoracic Stent Graft is a single-use device that is provided sterile. Sterilization is accomplished using 100% Ethylene Oxide. The sterilization process, equipment, and facility were found to be acceptable and a Sterility Assurance Level (SAL) of 10^{-6} was achieved. Product and package stability testing of the Talent™ Abdominal Stent Graft was performed and validated for a 2-year shelf life.

X. SUMMARY OF CLINICAL STUDIES

Medtronic performed a clinical study to establish a reasonable assurance of safety and effectiveness of endovascular treatment of descending thoracic aortic aneurysms with the Talent™ Thoracic Stent Graft System for the endovascular repair of fusiform aneurysms and saccular aneurysms/penetrating ulcers of the descending thoracic aorta in patients having appropriate anatomy in the U.S. under an investigational device exemption (IDE) study. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The VALOR Pivotal Study (VALOR Test Group) was a multi-center, non-randomized clinical study conducted within the U.S. to evaluate the safety and effectiveness of the Talent™ Thoracic Stent Graft System when used in the treatment of subjects with descending thoracic aortic aneurysms (fusiform aneurysms and saccular aneurysms/penetrating ulcers).

For the VALOR Test Group, 38 sites enrolled a total of 195 subjects. In the VALOR Test Group, analysis of the primary endpoints used follow-up visits at 1, 6 and 12 months after the implant procedure and annually for a total of 5 years from the date of the initial implant. Clinical sites sent CT/MR and chest X-ray (CXR) images to an independent Core Laboratory to provide an assessment of patient data through one year post implantation. All major adverse events (MAEs) were adjudicated by an independent Clinical Events Committee (CEC) for device and procedure relatedness.

The primary safety endpoint was All-Cause Mortality at one year. The All-Cause Mortality rate of TAA repair with the Talent™ Thoracic Stent Graft was to be compared to the literature All-Cause Mortality rate for open surgical TAA repair, within one year of the initial procedure (29.8%). In addition, safety outcomes for the Talent™ Thoracic Stent Graft were compared to the retrospective surgical comparator group described below.

Original Literature Control

The original literature control compared the All-Cause Mortality rate of TAA repair of the Talent™ Thoracic Stent Graft with the literature All-Cause Mortality rate for open surgical TAA repair, within one year of the initial procedure. Based on the adequacy of information regarding disease etiology, length of follow-up information and definition of events, three articles were chosen, from which 608 subjects had atherosclerotic lesions that accurately fit the VALOR Test Group's intended patient population of descending thoracic aortic aneurysms. Of the 608 patients, the number of patients surviving at 12 months was estimated from the 12 month rates given in the Kaplan-

Meier curves included in each article. Using this method, 181 patients were estimated to have died within one year, establishing an All-Cause Mortality rate of 29.8%.

Retrospective Open Surgery Group (Comparator Group)
After the original VALOR Trial was conducted, additional retrospective open surgical data were gathered from selected surgical centers to serve as a comparator for Acute Procedural Outcomes and Acute Adverse Events, as well as to further compare early and 12-Month Mortality and Aneurysm-Related Mortality. This Retrospective Open Surgery Group included 189 subjects from 3 centers who matched selected inclusion/exclusion criteria of the VALOR study. The VALOR Test and Retrospective Open Surgery Groups included surgical candidates diagnosed with a thoracic aortic aneurysm of degenerative etiology. The VALOR Test Group candidates were of low to moderate risk (Society of Vascular Surgery (SVS) risk levels 0, 1, and 2).

The primary effectiveness endpoint, Successful Aneurysm Treatment[2], was compared to a fixed rate of 80%, the lowest success rate consistent with the results from the control population described below. The effectiveness measure of 80% had also been used for the previously approved thoracic endograft.

Effectiveness Control
The control population for the primary effectiveness endpoint was derived from the 21 subjects who had reached 1 year of follow-up from both the high risk and low risk feasibility studies at the time.

B. Subject Accountability and Follow-up

For the VALOR Test Group, 38 sites enrolled a total of 195 subjects. One (1) subject had technical failure and did not receive a stent graft and therefore did not have any imaging follow-up. Four (4) subjects died and one (1) withdrew from the study before the 1-month visit.

There were 189 subjects eligible for clinical and imaging follow-up at 1-month follow-up interval. Of these 189 subjects, 80.4% (152/189) had a clinical follow-up. Please note; three (3) additional subjects who were not eligible for clinical follow-up had imaging follow-up within the expanded time windows (as footnoted within Table 6 below).

At the 6-month follow-up interval, 173 subjects were eligible for clinical and imaging follow-up. Of these, 74.0% (128/173) had clinical follow-up and 73.8 % (127/173) had imaging follow-up. CT imaging was performed on 68.2% (118/173) subjects.

At the 12-month follow-up interval, 157 subjects were eligible for clinical and imaging follow-up. Of these, 71.3% (112/157) had clinical follow-up and 90.4% (142/157) had imaging

[2] Successful Aneurysm Treatment, was a composite endpoint consisting of:

- No aneurysm growth greater than 5 mm at the 12 month follow-up visit when compared to the one (1) month follow-up visit as assessed by the Core Lab (after the initial Talent™ Thoracic Stent Graft implant); and
- Absence of a Type I endoleak as assessed by the Core Lab for which a secondary procedure was performed before, at or as a result of the 12 month follow-up visit.

follow-up. CT imaging was performed on 82.8% (130/157) subjects. Detailed subject accountability for 1, 6, and 12 months is provided in Table 6.

Table 6: Subject and Imaging Accountability Table– VALOR Test Group Only

Treatment / Follow-up Interval	Patient follow-up			Patients with imaging performed at time interval (Core Lab)		Patients with adequate imaging to assess the parameter				Patient events occurring before next visit[2]				
	Eligible	Clinical Follow-up[2]	Imaging Follow-up[3]	CT Imaging[3]	KUB Imaging[3]	Aneurysm size increase[3]	Endoleak[3]	Migration[4]	Integrity[3]	Technical Failure	Conversion to Surgery	Death	Withdrawal	Lost to Follow-up
Originally Enrolled	195									1				
Events after implant but before 1-month visit											0	4	1	0
Events at 1-month visit	189	152	192	184	189		174	182	161					
Events after 1-month visit but before 6-month visit											0	14	2	0
Events at 6-month visit	173	128	127	118	114	117	112	117	93					
Events after 6-month visit but before 12-month visit											1	13	1	1
Events at 12-month visit	157	112	142	130	125	129	123	129	97					

1 - Data analysis sample size varies for each of the timepoints above and in following tables. This variability is due to patient availability for follow-up, as well as, quantity and quality of images available from specific timepoints for evaluation. For example, the number and quality of images available for evaluation of endoleak at 6 months is different than the number and quality of images available at 12 months due to variation in the number of image exams performed, the number of images provided from the clinical site to the Core Lab, and/or the number of images with acceptable evaluation quality.

2 - Protocol-defined time windows were used for clinical follow-up and patient events:

- 1-month: 16days to 44 days
- 6 month: 153 days to 213 days
- 12-month: 335 days to 395 days

3 - Expanded time windows were used for Imaging follow-up and assessment of imaging-dependant parameters:

- 1-month: 0 days to 122 days
- 6 month: 153 days to 213 days
- 12-month: 335 days to 480 days for CT, Endoleak and Aneurysm size increase
- 335 days to 760 days for X-ray and Integrity.

4 - Number of subjects evaluable for migration assessment were based on CT performed in windows and Slice interval and thickness <5mm for 10mm evaluation.

C. Demographics and Baseline Medical History

Tables 7 through 10 provide the demographics of the VALOR Test Group subjects and the Retrospective Open Surgery Group.

Table 7: Subject Demographics: VALOR Test Group vs. Retrospective Open Surgery Group

	VALOR Test Group	Retrospective Open Surgery	p-value
Total Population Age			
N	195	189	
Mean ± SD (years)	70.2 ± 11.1	69.6 ± 9.1	0.528
Median	73.0	71.0	
Min-Max	27 - 86	27 - 85	
Male Age			
N	115	99	
Mean ± SD (years)	69.3 ± 11.7	69.9 ± 8.5	0.680
Median	72.0	71.0	
Min-Max	27 - 85	40 - 84	
Female Age			
N	80	90	
Mean ± SD (years)	71.6 ± 10.1	69.3 ± 9.8	0.130
Median	74.0	71.0	
Min-Max	38 - 86	27 - 85	
Gender			
Males	59.0% (115)	52.4% (99)	0.218
Females	41.0% (80)	47.6% (90)	
Ethnicity			
White, non-Hispanic	83.1% (162)	93.7% (177)	0.007
Black- non-Hispanic	12.8% (25)	5.8% (11)	
Hispanic (White or Black)	2.6% (5)	0.5% (1)	
Asian/Pacific Islander	1.0% (2)	0% (0)	
Native American	0% (0)	0% (0)	
Other	0.5% (1)[1]	0% (0)	
1 - One subject had Ethnicity specified as "None given."			

Table 8: Subject Anatomic Lesion Type for VALOR Test Group

Thoracic Lesion[1]	VALOR Test Group - N (%)
Fusiform	112 (57.4%)
Saccular/Penetrating Ulcer	70 (35.9%)
Both	13 (6.7%)
1- The Retrospective Open Surgery Group did not provide patient level data for the anatomic lesion type treated.	

Table 9: Baseline Medical History: VALOR Test Group vs. Retrospective Open Surgery Group

Body System / Condition	VALOR Test Group % (m/n)[1] N = 195	Retrospective Open Surgery % (m/n)[1] N = 189	p-value
Cardiovascular			
Angina	14.4% (28/195)	22.8% (26/114)	0.064
Arrhythmias	26.7% (52/195)	20.3% (37/182)	0.182
Carotid artery disease	5.6% (11/195)	Not Available	N/A
Congestive heart failure (CHF)	8.7% (17/195)	11.2% (21/187)	0.495
Coronary artery bypass grafting (CABG)	10.3% (20/195)	13.3% (25/188)	0.428
Coronary artery disease (CAD)	40.5% (79/195)	49.2% (91/185)	0.099
Hypertension	87.2% (170/195)	88.8% (166/187)	0.641
Myocardial infarction (MI)	13.8% (27/195)	20.9% (39/187)	0.079
Percutaneous coronary intervention (PCI)	5.6% (11/195)	Not Available	N/A
Peripheral vascular disease (PVD)	16.4% (32/195)	37.4% (70/187)	<0.001
Symptomatic thoracic aortic aneurysm	26.2% (51/195)	Not Available	N/A
Abdominal Aortic Aneurysm (AAA)	19.0% (37/195)	37.0% (70/189)	<0.001
Abdominal Aortic Aneurysm Repair	2.1% (4/195)	27.5% (52/189)	<0.001
Gastrointestinal conditions	53.8% (105/195)	Not Available	N/A
Renal insufficiency	17.4% (34/195)	16.0% (30/187)	0.784
Musculoskeletal conditions	53.8% (105/195)	Not Available	N/A
Neurological			
Cerebral vascular accident (CVA)	9.7% (19/195)	13.4% (25/186)	0.267
Paraplegia	1.0% (2/195)	0.5% (1/186)	1.000
Paraparesis	0.5% (1/195)	Not Available	N/A
Transient ischemic attack (TIA)	7.7% (15/195)	Not Available	N/A
Pulmonary			
Chronic obstructive pulmonary disease	36.9% (72/195)	42.6% (80/188)	0.296
Tobacco use	76.9% (150/195)	75.9% (142/187)	0.904
Other abnormal body systems			
Hyperlipidemia	43.6% (85/195)	Not Available	N/A
Diabetes	15.9% (31/195)	8.6%	0.030
Bleeding disorders	2.6% (5/195)	Not Available	N/A

1 - m = number in category, n = number of known values

Table 10: Baseline Modified SVS Classification: VALOR Test Group

	n	SVS 0 % (m)	SVS 1 % (m)	SVS 2 % (m)	SVS 3 % (m)
Modified SVS[1]	195	4.1% (8)	21.0% (41)	72.8% (142)	2.1% (4)

1 - SVS Medical Co-Morbidity Grading System for SV3 Modified for Age (>85), Uncontrolled Hypertension and Cardiac MI within 6 months with no intervention.

D. Baseline Aneurysm Data

Table 11 lists the initial aneurysm diameter sizes treated. Table 12 lists the baseline dimensions of the vessels treated.

Table 11: Baseline Maximum Aneurysm Diameters: VALOR Test Group vs. Retrospective Open Surgery Group

Aneurysm Diameter (mm)	VALOR Test Group		Retrospective Open Surgery %(m/n)	p-value Site-Reported VALOR vs. Retrospective Open Surgery[3]
	Site-Reported % (m/n)[1]	Core-Lab Reported % (m/n)[2]		
10-17	0% (0/188)	0% (0/187)	0% (0/189)	<0.001
18-29	0% (0/188)	0.5% (1/187)	0% (0/189)	
30-39	4.3% (8/188)	7.5% (14/187)	0% (0/189)	
40-49	10.6% (20/188)	20.3% (38/187)	0.5% (1/189)	
50-59	34.6% (65/188)	34.8% (65/187)	13.8% (26/189)	
60-69	33.5% (63/188)	24.6% (46/187)	40.7% (77/189)	
70-79	12.2% (23/188)	10.2% (19/187)	24.3% (46/189)	
80-89	3.2% (6/188)	2.1% (4/187)	16.9% (32/189)	
90-99	1.1% (2/188)	0% (0/187)	0.5% (1/189)	
100-109	0.5% (1/188)	0% (0/187)	1.6% (3/189)	
110-119	0% (0/188)	0% (0/187)	0.5% (1/189)	
120+	0% (0/188)	0% (0/187)	1.1% (2/189)	

1 - Denominator is 188 subjects with site reported data.
2 - Denominator is 187 subjects with evaluable scans.
3 - This p-value represents a Monte Carlo estimate of the p-value for the exact Mantel-Haenszel Chi-Square test for trend, based on 100,000 Monte Carlo repetitions.

Table 12: Baseline Vessel Dimensions (Core Lab Reported): VALOR Test Group Only

Vessel Dimensions (mm)	n[1]	Mean ± SD	Median	Min	Max
Proximal neck diameter	187	31.2 ± 4.9	31.5	18.5	43.5
Aneurysm diameter	187	55.5 ± 11.6	56.0	26.2	88.8
Distal neck diameter	184	29.7 ± 5.0	29.5	17.0	42.5
Proximal neck length	187	80.0 ± 52.1	77.9	10.0	234.0
Aneurysm length	180	121.4 ± 72.7	107.7	8.0	297.5
Distal neck length	184	90.0 ± 62.9	73.5	9.0	255.0
Right external iliac minimum diameter	122	6.5 ± 1.5	6.5	2.9	11.0
Left external iliac minimum diameter	124	6.6 ± 1.5	6.5	3.3	10.9

1- Denominators are n specified from readable scans.

E. Baseline Devices Implanted Data

Table 13 provides details on the number of devices implanted per subject for the VALOR Test Group.

Table 13: Number of Talent™ Thoracic Devices Implanted at Initial Procedure

Devices Implanted	
Number per subject	**% (m)[1]**
0	0.5% (1)
1	19.5% (38)
2	28.7% (56)
3	24.6% (48)
4	17.4% (34)
5	7.2% (14)
6	1.5% (3)
7+	0.5% (1)
1- m= number of subjects implanted & percentages based on total number of enrolled subjects (N=195)	

Table 14 cross-tabulates the 194 subjects in the VALOR Test Group who had Talent™ Stent Grafts implanted by the number of main sections and the number of extensions. For example, 38 subjects had a single main section implanted and no extensions, and 5 subjects had one main section and one extension. Similarly, 51 subjects had two main sections and no extensions and 6 had two main sections and one extension.

Table 14: Number of Main Sections and Number of Extensions Implanted at Initial Procedure: VALOR Test Group Only

m (%)[1]		Number of Extensions			
		0	1	2	Total
Number of Main Sections	1	38 (19.59%)	5 (2.58%)	1 (0.52%)	44 (22.68%)
	2	51 (26.29%)	6 (3.09%)	5 (2.58%)	62 (31.96%)
	3	41 (21.13%)	11 (5.67%)	2 (1.03%)	54 (27.84%)
	4	18 (9.28%)	6 (3.09%)	0 (0.00%)	24 (12.37%)
	5	6 (3.09%)	1 (0.52%)	0 (0.00%)	7 (3.61%)
	6	2 (1.03%)	1 (0.52%)	0 (0.00%)	3 (1.55%)
	Total	156 (80.41%)	30 (15.46%)	8 (4.12%)	194 (100.00%)
1 – m = number of subjects with tabulated number of main sections and extensions. Percentages based on total number of implanted subjects (N=194)					

Table 15 provides details on the components (proximal main devices, proximal extension devices, distal main devices, and distal extension devices) implanted per subject for the VALOR Test Group.

Table 15: Talent™ Thoracic Stent Graft Devices Implanted

Diameter (mm)	Stent Graft Modular Component (Number Implanted)		
	Proximal Main % (m)[1]	Proximal Extension % (m)[1]	Distal Extension % (m)[1]
22	0.5% (1)		
24	1.4% (3)		
26	1.9% (4)	0.0% (0)	0.0% (0)
28	2.8% (6)	0.0% (0)	12.0% (3)
30	3.8% (8)	4.8% (1)	4.0% (1)
32	8.1% (17)	14.3% (3)	8.0% (2)
34	11.4% (24)	4.8% (1)	16.0% (4)
36	16.1% (34)	14.3% (3)	8.0% (2)
38	19.4% (41)	19.0% (4)	16.0% (4)
40	11.4% (24)	4.8% (1)	12.0% (3)
42	10.9% (23)	4.8% (1)	8.0% (2)
44	5.2% (11)	9.5% (2)	8.0% (2)
46	7.1% (15)	23.8% (5)	8.0% (2)
Total Catalog Devices Implanted	211	21	25

1 - m =number of subjects implanted with specific type of device within each diameter category & denominator is the total number of the specific type of device implanted.

F. Safety Results

Primary Safety Endpoints

All-Cause Mortality at One Year: VALOR Test Group vs. Original Literature Control

The primary safety endpoint was All-Cause Mortality at 12 months. Based on the test of superiority of the All-Cause Mortality rate in the Test Group to that of the original literature control group with an All-Cause Mortality rate of 181 of 608 subjects, or 29.8% (H_0: $P_{TestArm} \geq P_{SurgicalGroup}$ versus H_A: $P_{TestArm} < P_{SurgicalGroup}$), the VALOR Test Group subjects met the pre-specified performance goal of 29.8%. The primary safety endpoint of the VALOR Study was met. Through one year, subjects who received the Talent™ Thoracic Stent Graft experienced an All-Cause Mortality rate of 16.1% and the subjects who underwent open surgery experienced a rate of 29.8%.

All-Cause Mortality at 30 days and 12 months: VALOR Test Group vs. Retrospective Open Surgery Group

Table 16 describes the 30-day mortality rates for the VALOR Test Group as compared to the Retrospective Open Surgery Group. The VALOR Test Group experienced a lower rate of early mortality (2% vs. 8%). An analysis of freedom from All-Cause Mortality was performed, and a Kaplan-Meier plot of subject freedom from All-Cause Mortality is provided in Table 17 and Figure 7.

Table 16: All-Cause Mortality at 30 Days and 12 months

	VALOR Test Group % (m/n)	Retrospective Open Surgery % (m/n)	95% Exact Confidence Interval of Difference[1,2]
All-cause mortality at 30 days	2.1% (4/195)	7.9% (15/189)	(-10.9%, -1.3%)
All-cause mortality at 12 months	16.1% (31/192)	20.6% (39/189)[3]	(-12.4%, -3.4%)

1 - Confidence level was not adjusted for multiplicity. Confidence interval for difference (VALOR Test Group – Retrospective Open Surgery group) in percentage was calculated by the exact method.
2 - Difference represents the (% of patients with mortality from any cause within the period in the population treated with the test device) - (% of patients with mortality from any cause within the period in the population treated with open surgery).
3 - Of the 39 deaths, this data includes both information from the reporting centers and queries of the National Social Security Death Index database.

Figure 7: KM Plot of All Cause Mortality at 30 Days and 12 Months: VALOR Test Group vs. Retrospective Open Surgery Group

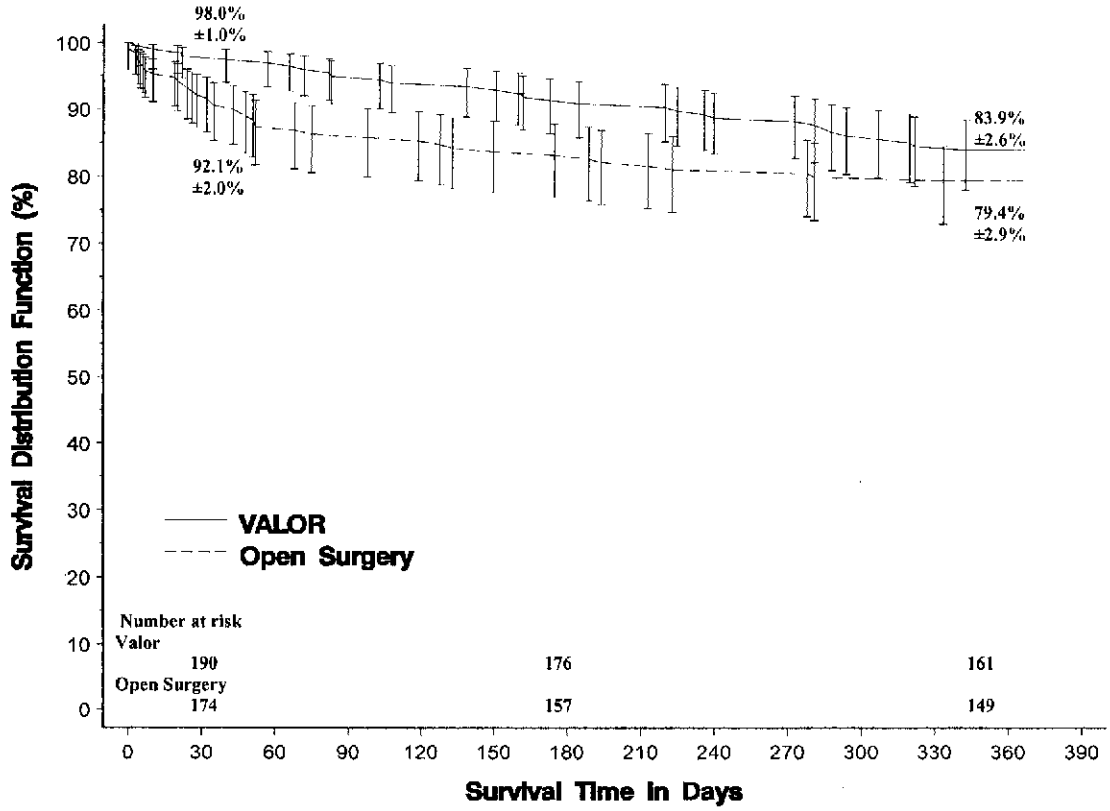


Table 17: Details of Kaplan-Meier Plot of Freedom from All Cause Mortality at 30 Days and 12 Months: VALOR Test Group vs. Retrospective Open Surgery Group

	VALOR Test Group			Retrospective Open Surgery		
	Treatment to 30 days	31 days to 182 days	183 days to 365 days	Treatment to 30 days	31 days to 182 days	183 days to 365 days
No. at Risk	195	190	176	189	174	157
No. of Events	4	13	14	15	17	7
No. Censored	1	1	1	0	0	1
Kaplan-Meier Estimate	0.980	0.912	0.839	0.921	0.831	0.794

Secondary Safety Endpoints

Major Adverse Events (MAE) at 30 days for VALOR Test Group vs. Retrospective Open Surgery Group

Adverse events were categorized by severity in the VALOR Trial and in the Retrospective Open Surgery Group using the following definitions. A Major Adverse Event (MAE) was defined as the occurrence of any of the following:

- Death:
  - due to complications of the procedure, including bleeding, vascular repair, transfusion reaction, or conversion to open surgical TAA repair
  - within 30 days of the baseline implant or surgical procedure
- Respiratory complications (atelectasis / pneumonia, pulmonary embolism, pulmonary edema, respiratory failure)
- Renal complications (renal failure, renal insufficiency)
- Cardiac: MI, unstable angina, new arrhythmia, exacerbation of congestive heart failure (CHF)
- Neurological: new CVA / embolic events, paraplegia / paraparesis
- Aneurysm rupture
- Gastrointestinal: bowel ischemia
- Major bleeding complication (procedural or post-procedural), coagulopathy
- Vascular complications.

Comparisons of the 30-day MAEs for the Talent™ Thoracic subjects versus the retrospective Open Surgical Group are further summarized in Figure 8 and Tables 18 through 20 below.

Table 18: Summary of MAEs for VALOR Test Group vs. Retrospective Open Surgery Group (30 days)

Category	VALOR Test Group Major Adverse Events 0-30 days % (m/n) N=195	Retrospective Open Surgery Major Adverse Events 0-30 days % (m/n) N=189[1]	95% Exact Confidence Interval of Difference[2,3]
Any MAE	41.0% (80/195)	84.4% (151/179)	(-51.9%, -34.2%)
Respiratory complications	13.3% (26/195)	46.9% (84/179)	(-42.2%, -24.6%)
Renal complications	6.2% (12/195)	29.1% (52/179)	(-30.6%, -15.3%)
Cardiac complications	12.3% (24/195)	44.7% (80/179)	(-41.0%, -23.5%)
Neurological complications	11.8% (23/195)	20.1% (36/179)	(-16.0%, -0.7%)
GI complications	1.0% (2/195)	0.6% (1/179)	(-2.1%, 3.2%)
Bleeding complications	15.4% (30/195)	48.0% (86/179)	(-41.7%, -23.4%)
Vascular complications	21.0% (41/195)	12.3% (22/179)	(1.1%, 16.5%)
Target Lesion Aneurysm Rupture	0.0% (0/195)	0.6% (1/179)	(-3.1%, 1.4%)

1 - 10 subjects were followed for less than 16 days without MAE so they were eliminated from the analysis.
2 - Confidence level was not adjusted for multiplicity. Confidence interval for difference (VALOR Test Group – Retrospective Open Surgery Group) in percentage was calculated by the exact method.
3 - Difference represents the (% of patients free from MAEs within 30 days in the population treated with the test device) - (% of patients free from MAEs within 30 days in the population treated with open surgery).

One or more MAEs were reported in 80 of the 195 VALOR Test Group subjects available for evaluation, resulting in a probability of freedom from MAEs of 59%. In the Retrospective Open Surgery group, 151 of the 179 subjects had one or more MAEs, resulting in a freedom from MAE rate of 15.6% in this group.

Table 19: Freedom from MAEs at 30 days: VALOR Test Group vs. Retrospective Open Surgery Group

Parameter	VALOR Test Group	Retrospective Open Surgery	95% Exact Confidence Interval of Difference[1,2]
Number of subjects at start	195	179	
Number of subjects with one or more events	80	151	
Probability of freedom from event	59.0%	15.6%	(34.2%, 51.9%)

1 - Confidence level was not adjusted for multiplicity. Confidence interval for difference (VALOR Test Group – Retrospective Open Surgery Group) in percentage was calculated by the exact method.
2 - Difference represents the (% of patients free from MAEs within 30 days in the population treated with the test device) - (% of patients free from MAEs within 30 days in the population treated with open surgery).

Figure 8: Kaplan-Meier Plot of Freedom from MAEs at 30 Days: VALOR Test Group vs. Retrospective Open Surgery Group

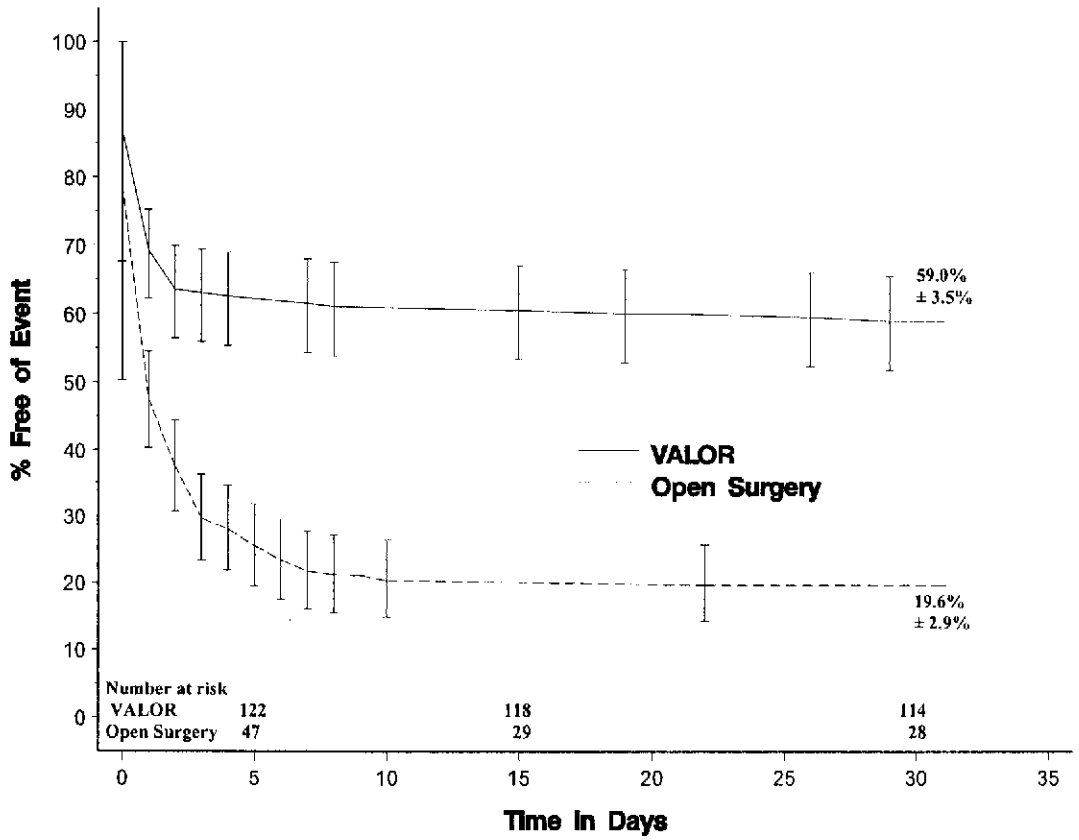


Table 20: Details of Kaplan-Meier Plot of Freedom from MAEs at 30 Days for VALOR Test Group vs. Retrospective Open Surgery Group

	VALOR Test Group			Retrospective Open Surgery		
	Treatment to 5 days	6 days to 15 days	16 days to 30 days	Treatment to 5 days	6 days to 15 days	16 days to 30 days
No. at Risk	195	122	118	189	47	29
No. of Events	73	4	3	141	9	1
No. Censored	0	0	1	1	9	0
Kaplan-Meier Estimate	0625	0.605	0.590	0.254	0.203	0.196

Serious Major Adverse Events at 30 days and 12 months: VALOR Test Group

VALOR MAEs were further stratified into more clinically severe events: Serious Major Adverse Events (Serious MAEs). These Serious MAEs were fatal, life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, caused persistent or significant disability/incapacity, or resulted in a congenital anomaly/birth defect.

MAEs were reviewed by the CEC and adjudicated as either device- and/or procedure-related as per the study protocol. A MAE that was identified as a Serious Adverse Event (SAE) by the clinical Investigator was defined as a Serious MAE. During the VALOR Study, 59 of 195 evaluable subjects had one or more Serious Major Adverse Events within 30 days, giving a rate of Serious MAEs within 30 days of 30.3% (95% CI 23.9-37.2%). Eighty-two (82) of 192 evaluable subjects had one or more Serious MAEs within 12 months, providing a Serious MAE rate of 42.7% (95% CI 35.6-50.0%). These data are further summarized in Figure 9 and Tables 21 through 23.

Table 21: Summary of Serious MAEs from VALOR Test Group Only

Category	0-30 days % (m) N=195	0-30 days 95% Exact CI[1]	0-365 days % (m) N=192	0-365 days 95% Exact CI[1]
	Serious Major Adverse Events		Serious Major Adverse Events	
Any Serious MAE	30.3% (59/195)	(23.9%, 37.2%)	42.7% (82/192)	(35.6%, 50.0%)
Respiratory complications	6.7% (13/195)	(3.6%, 11.1%)	15.1% (29/192)	(10.4%, 21.0%)
Renal complications	3.6% (7/195)	(1.5%, 7.3%)	6.8% (13/192)	(3.7%, 11.3%)
Cardiac complications	5.1% (10/195)	(2.5%, 9.2%)	12.0% (23/192)	(7.7%, 17.4%)
Neurological complications	9.7% (19/195)	(6.0%, 14.8%)	13.5% (26/192)	(9.0%, 19.2%)
GI complications	0.5% (1/195)	(0.0%, 2.8%)	1.0% (2/192)	(0.1%, 3.7%)
Bleeding complications	13.3% (26/195)	(8.9%, 18.9%)	14.6% (28/192)	(9.9%, 20.4%)
Vascular complications	9.2% (18/195)	(5.6%, 14.2%)	10.4% (20/192)	(6.5%, 15.6%)
Target Lesion Aneurysm Rupture	0.0% (0/195)	(0.0%, 1.9%)	0.5% (1/192)	(0.0%, 2.9%)
1 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.				

Table 22: Freedom from Serious MAEs at 30 days and 12-months - VALOR Test Group

Parameter	Talent™ Thoracic	
	Serious MAE at 30 days	Serious MAE at 12-months
Number of subjects at start	195	192[1]
Number of subjects with one or more events	59	82
Probability of freedom from event	69.7%	57.3%
Exact 95% confidence interval for freedom from event[2]	(62.7%, 76.1%)	(49.1%, 63.4%)
1 -192 subjects followed for the required time frame. 2 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.		

Figure 9: Kaplan-Meier Plot of Freedom from Serious MAEs: VALOR Test Group Only

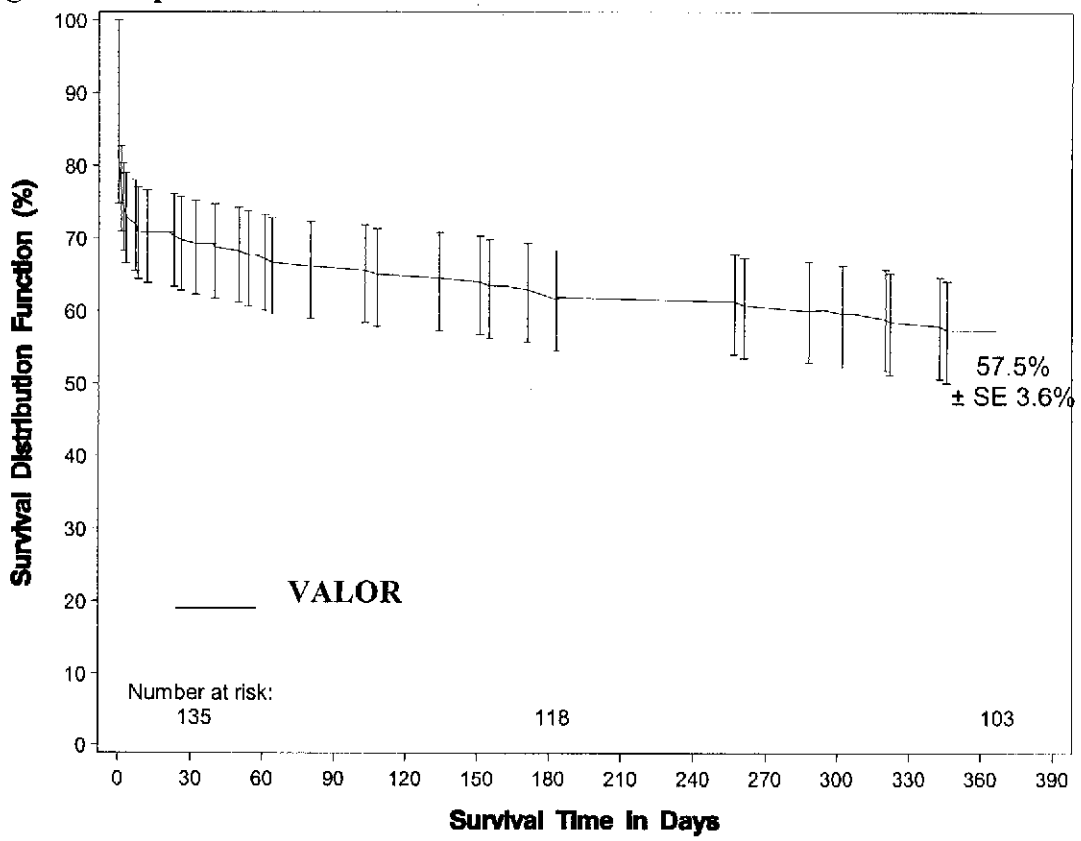


Table 23: Details of Kaplan-Meier Plot of Freedom from Serious MAEs: VALOR Test Group Only

	VALOR Test Group		
	Treatment to 30 days	31 days to 182 days	183 days to 365 days
No. at Risk	195	135	118
No. of Events	59	13	10
No. Censored	1	4	5
Kaplan-Meier Estimate	0.697	0.629	0.575

Aneurysm-Related Mortality

Table 24 provides Aneurysm-Related Mortality information for the VALOR Test and Retrospective Open Surgery Groups. A Kaplan-Meier plot of subject freedom from Aneurysm-Related Mortality is provided in Figure 10, and an analysis of freedom from Aneurysm-Related Mortality was provided in Table 25.

Table 24: Aneurysm-Related Mortality at 12 Months: VALOR Test Group vs. Retrospective Open Surgery

	VALOR Test Group[1] % (m/n)	Retrospective Open Surgery[2] % (m/n)	95% Exact Confidence Interval of Difference[3,4]
Aneurysm-Related Mortality at 12 Months	3.1% (6/192)	11.6% (22/189)	(-14.2%, -2.9%)

1 - Aneurysm-related mortality was defined as any death within 30 days from initial. implantation or occurring as a consequence of an aneurysm rupture, a conversion to open repair, or any other secondary endovascular procedure relative to the aneurysm that was treated by the Talent™ Thoracic Stent Graft System as evidenced by CT, angiography or direct observation at surgery or autopsy. Excluded are aneurysms in anatomic areas other than the targeted segment treated by the Talent™ Thoracic Stent Graft System.

2 - The definition for Aneurysm Related Mortality for the Retrospective Open Surgery Group was any death within 30 days from the surgical procedure or any death caused by re-intervention of the targeted aortic segment, or by complications related to the graft or the procedure (e.g., graft infections, rupture, pseudoaneurysm, aorto-eophageal fistula, aorto-bronchial fistula).

3 - Confidence level was not adjusted for multiplicity. Confidence interval for difference (VALOR Test Group – Retrospective Open Surgery Group) in percentage was calculated by the exact method.

4 - Difference represents the (% of patients with aneurysm-related mortality within 12 months in the population treated with the test device) - (% of patients with aneurysm-related mortality within 12 months in the population treated with open surgery).

Figure 10: Kaplan-Meier Plot of Freedom from Aneurysm-Related Mortality: VALOR Test Group vs. Retrospective Open Surgery Group

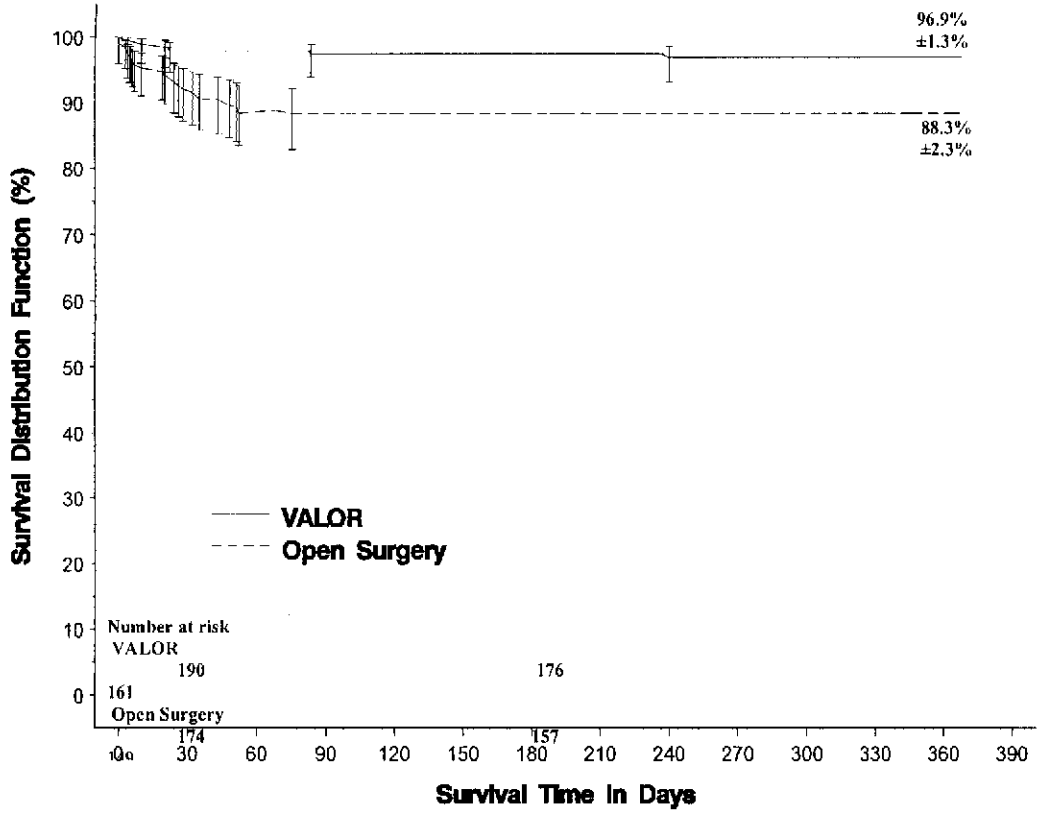


Table 25: Details of Kaplan-Meier Plot of Freedom from Aneurysm-Related Mortality at 12 Months: VALOR Test Group vs. Retrospective Open Surgery Group

	VALOR Test Group			Retrospective Open Surgery		
	Treatment to 30 days	31 days to 182 days	183 days to 365 days	Treatment to 30 days	31 days to 182 days	183 days to 365 days
No. at Risk	195	190	176	189	174	157
No. of Events	4	1	1	15	7	0
No. Censored	1	13	14	0	10	8
Kaplan-Meier Estimate	0.980	0.974	0.969	0.921	0.883	0.883

G. Effectiveness Results

Primary Effectiveness Endpoint: Aneurysm-Related Mortality at 12 Months

The primary effectiveness endpoint, which was Successful Aneurysm Treatment, was met. This endpoint was a composite endpoint defined by:

- no aneurysm growth greater than 5 mm at the 12-month follow-up visit when compared to the 1-month follow-up visit as assessed by the Core Lab (after the initial Talent™ Thoracic Stent Graft implant); and
- absence of a Type I endoleak as assessed by the Core Lab for which a secondary procedure was performed before, at or as a result of the 12-month follow-up visit.

The rate of Successful Aneurysm Treatment in the VALOR Test Group, 89.2%, was higher than the 80% comparator (which was based on earlier feasibility studies). As shown in Table 26, the Talent™ Thoracic Stent Graft achieved a successful aneurysm treatment rate of 89.2%. Table 27 provides details regarding subjects who have failed the successful aneurysm treatment endpoint.

Table 26: Successful Aneurysm Treatment: VALOR Test Group

Primary Effectiveness Endpoint	% (m / n) [95% CI]	95% Exact Confidence Interval[2]
Successful Aneurysm Treatment at 12 months	89.2% (116/130)[1]	[82.6% – 94.0%]
1 - Eligible subjects for Successful Aneurysm Treatment required images depicting a one and twelve month aneurysm size, or had a Type I endoleak which required endovascular repair to be included in the analysis. Twenty-nine (29) subjects were missing a 12 month image at the Core Lab and were excluded from this analysis. 2 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.		

Table 27: Summary of Subjects with Primary Effectiveness Failure: VALOR Test Group

Subjects with Primary Effectiveness Failure	n
Aneurysm growth > 5mm	10[1]
Type I endoleak requiring re-intervention	3
Aneurysm growth > 5mm and Type I endoleak requiring re-intervention	1[2]
1 - Of the 10 subjects, four (4) had secondary procedures. Of the remaining six (6) subjects, one (1) patient died of cardiac arrest at approximately 24 months, and one died of cirrhosis at 14 months. 2- This subject is alive at 24 months.	

Other Effectiveness Data

Table 28 summarizes the other secondary endpoints from the VALOR Test Group.

Table 28: Other Effectiveness Data for VALOR Test Group

Secondary Endpoint	Incidences % (m / n)	95% Exact CI[1]
Successful deployment and delivery of the stent graft at implantation	99.5% (194/195)[2]	(97.2%, 100.0%)
Secondary procedures due to endoleak at 30 days	0.0% (0/194)	(0.0%, 1.9%)
Conversion to open surgical repair within 12 months post-implantation	0.5% (1/192)[3]	(0.0%, 2.9%)
Aneurysm rupture within 12 months post-implantation	0.5% (1/192)[4]	(0.0%, 2.9%)
Stent graft migration between 1 and 12 months	3.9% (4/103)[5]	(1.1%, 9.6%)
Proximal stent graft migration > 10 mm proximally	0.0% (0/103)	(0.0%, 3.5%)
Proximal stent graft migration > 10 mm distally	1.9% (2/103)	(0.2%, 6.8%)
Distal stent graft migration > 10 mm proximally	1.9% (2/103)	(0.2%, 6.8%)
Distal stent graft migration > 10 mm distally	0.0% (0/103)	(0.0%, 3.5%)
All endoleaks at 12 months (Core Lab reported)	12.2% (15/123)	(7.0%, 19.3%)
Type I	4.9% (6/123)[6]	(1.8%, 10.3%)
Type II	4.9% (6/123)[7]	(1.8%, 10.3%)
Type III	0.0% (0/123)	(0.0%, 3.0%)
Type IV	0.0% (0/123)	(0.0%, 3.0%)
Unknown	2.4% (3/123)	(0.5%, 7.0%)
Secondary procedures due to endoleak between 31 days and 365 days	6.5% (12/186)[8]	(3.4%, 11.0%)
Loss of patency of the stent graft at 12 months	0% (0/107)	(0.0%, 3.4%)
Loss of stent graft integrity at 12 months[9]	2.1% (2/97)[10]	(0.3%, 7.3%)
Change in maximum aneurysm diameter from 1 month image		
Increase > 5 mm	8.5% (11/129)	(4.3%, 14.7%)
Stable	67.4% (87/129)	(58.6%, 75.4%)
Decrease > 5 mm	24.0% (31/129)	(16.9%, 32.3%)

1 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.

2 - One (1) subject did not receive a stent graft due to extensive disease and heavy calcification of the iliac arteries.

3 - One (1) subject was converted to surgery. The stent graft was explanted 9 months post initial procedure due to an apparent infection in the stented segment of the aorta.

4 - One (1) subject experienced aneurysm rupture at the distal thoracic aorta, at the stent graft seal zone. Review of CT scans by the Core Lab revealed patient had a thoraco-abdominal aneurysm rather than an isolated descending thoracic aneurysm as well as an inadequate distal landing zone.

5 - Migration is defined as proximal or distal movement of the stent graft (>10mm) relative to fixed anatomic landmarks. The 1-month CTA/MRA was used as the baseline for this determination.

- Two (2) subjects had no MAEs due to their device migration.
- One (1) subject underwent a secondary procedure at Day 273. Two additional proximal main devices were implanted to resolve migration and cover a pseudoaneurysm. Repair was successful
- One (1) subject had no MAEs due to their device migration. Subject underwent a planned AAA open repair at approximately 2 months and expired at approximately 14 months from cirrhosis.

Secondary Endpoint	Incidences % (m / n)	95% Exact CI[1]
6 - None of the six (6) subjects with Type I endoleak underwent secondary procedure within 12 months 7 - One (1) of the six (6) subjects with Type II endoleak underwent a secondary procedure at 140 days 8 - The 12 subjects who received a secondary endovascular procedure are characterized as follows, all secondary repairs were successful: • Two (2) patients had endoleaks detected at day 6 and 35, with secondary procedures at Day 84 and 186, respectively. Proximal mains were placed to correct Type I endoleaks (proximal). • One (1) patient had endoleak detected at day 55, with secondary procedure at Day 334. Proximal extension was placed to correct Type I endoleak (proximal). • Four (4) patients had endoleak detected at days 22, 29, 33 and 38, with secondary procedures at Day 140, 203, 116 and 253, respectively. Distal extensions were placed to correct three Type I endoleaks (distal) and one Type II endoleak. • One (1) patient had endoleak detected at day 8, with secondary procedure at Day 113. Distal mains were placed to correct a Type III endoleak. • Three (3) patients had endoleaks detected at day 19, 27 and 32, with secondary procedures at Day 56, 49 and 42, respectively. Proximal and distal mains were placed to correct one Type I (distal) endoleak and two Type I (proximal) endoleaks. • One (1) patient had endoleak detected at day 155, with secondary procedure at Day 246. Proximal and Distal extensions were placed to correct a Type I (proximal) endoleak. 9 - Loss of stent graft integrity is defined as the absence of stent fractures and/or graft fabric defects. 10 - Of the two (2) subjects with loss of stent graft integrity, one was due to a nitinol spring fracture and the second was a connecting bar fracture. Neither subject had any adverse event related to these fractures. Both subjects are alive at 24 months.		

H. Supplemental Acute Procedural Data

Table 29 provides the Acute Procedural Data for VALOR Test Group and Retrospective Open Surgery Group. The VALOR Test Group showed reduced blood loss, reduced need for transfusions, as well as shorter ICU and hospital stays when compared to open surgery.

Table 29: Supplementary Acute Procedural Data

Parameter	VALOR Test Group	Retrospective Open Surgery	95% Confidence Interval of Difference[5,6]
Subjects requiring blood transfusion (%)	22.7% (44/194)	93.7% (164/175)	(-77.5%, -63.5%)
Blood loss during procedure (ml) (mean ± SD)[1]	371.2 ± 514.4	3054.9 ± 1702.4	(-2961.1, -2406.2)
Duration of implant procedure (min) (mean ± SD)[2]	154.2 ± 76.0	303.3 ± 97.6	(-166.9, -131.3)
Time in Intensive Care Unit (hours) for all assessable subjects (mean ± SD)[3]	46.8 ± 114.3	185.3 ± 204.7	
Overall hospital stay (days) (mean ± SD)[4]	6.4 ± 11.5	16.7 ± 15.0	(-12.9, -7.5)

1 - 189 VALOR Test Group subjects and 57 Retrospective Open Surgery subjects had known data for this parameter.
2 - 194 VALOR Test Group subjects and 178 Retrospective Open Surgery had known data for this parameter.
3 - 193 VALOR Test Group subjects and 168 Retrospective Open Surgery had known data for this parameter.
4 - 195 VALOR Test Group subjects and 186 Retrospective Open Surgery had known data for this parameter.
5 - Confidence level was not adjusted for multiplicity. Confidence intervals for difference (VALOR Test Group-Retrospective Open Surgery group) in means were calculated using a t-distribution. Confidence intervals for difference (VALOR Test Group-Retrospective Open Surgery group) in percentages were calculated by the exact method. Confidence interval for Time in ICU is not calculated due to a large number of ties in the data (i.e. large number of "0 hours" reported in the Test Group).
6 - For Duration of Procedure and Overall Hospital Stay, difference represents the (mean of specific acute procedural parameter in the population treated with the test device) - (mean of specific acute procedural parameter in the population undergoing open surgical repair). For Patients Requiring Blood Transfusion, difference represents the (% of patients with the specific acute procedural parameter for the population treated with the test device) - (% of patients with the specific acute procedural parameter for the population undergoing open surgical repair).

I. Evaluation of Gender Bias

To more carefully evaluate the possible gender-based differences in outcome of treatment with the Talent™ Thoracic Stent Graft, a gender subset analysis was performed on safety and effectiveness outcomes within the VALOR Test Group. Female and male subjects had very similar all-cause mortality at 12 months (the Primary Safety Endpoint): 15.2% and 16.8%, respectively, for an overall rate of 16.1%. Successful aneurysm treatment at 12 months (the Primary Effectiveness Endpoint) was 98.2% in females and 82.4% in males for an overall rate of 89.2%. These findings indicate a nearly equal safety outcome for males and females and a higher successful aneurysm treatment rate for female subjects. Additional analyses of the performance of this device in female patients will be conducted as part of a post-approval study.

J. VALOR Test Group Results by Lesion Type

The VALOR Test Group consisted of subjects with the following three groups of lesion types:

- Subjects with fusiform thoracic aneurysms
- Subjects with saccular aneurysms and/or penetrating ulcers
- Subjects with multiple types of lesions (fusiform thoracic aneurysms and saccular and/or penetrating ulcers).

Demographic and lesion characteristics, as well as safety and effectiveness endpoint analysis by lesion type, are provided below in Tables 30 through 36. Although the safety and effectiveness results of each of the separate lesion types support the poolablity of the data, this information is provided for completeness sake and for physician reference.

Subject Demographics and Lesion Characteristics

Table 30: Subject Demographics by Lesion Type – VALOR Test Group Only

	Fusiform	Saccular/ Penetrating Ulcer	Multiple Lesion
Age for Total Population			
N	112	70	13
Mean ± SD (years)	71.7 ± 9.2	68.0 ± 13.4	69.4 ± 11.9
Median	74.0	72.0	74.0
Min-Max	39 – 86	27 – 85	46 – 85
Male			
N	63	44	8
Mean ± SD (years)	70.7 ± 8.9	67.8 ± 14.6	67.1 ± 13.9
Median	73.0	72.0	72.5
Min-Max	50 – 85	27 – 85	46 – 85
Female			
N	49	26	5
Mean ± SD (years)	73.1 ± 9.3	68.5 ± 11.5	73.0 ± 7.8
Median	75.0	70.5	75.0
Min-Max	39 – 86	38 – 82	64 – 84
Gender			
Males	56.3% (63)	62.9% (44)	61.5% (8)
Females	43.8% (49)	37.1% (26)	38.5% (5)
Ethnicity			
White, non-Hispanic	84.8% (95)	81.4% (57)	76.9% (10)
Black- non-Hispanic	12.5% (14)	12.9% (9)	15.4% (2)
Hispanic (White or Black)	1.8% (2)	2.9% (2)	7.7% (1)
Asian/Pacific Islander	0% (0)	2.9% (2)	0% (0)
Native American	0% (0)	0% (0)	0% (0)
Other	0.9% (1)[1]	0% (0)	0% (0)
1- One subject declined providing ethnicity			

Table 31: Baseline Vessel Dimensions by Lesion Type: VALOR Test Group Only (Core Lab Reported[1])

Vessel Dimension	n	Mean ± SD	Median	Min	Max
Proximal Neck Diameter (mm)					
Fusiform	107	32.1 ± 4.7	32.5	19.0	43.5
Saccular/Penetrating Ulcer	67	29.8 ± 5.2	30.5	18.5	43.5
Multiple Lesion	13	31.0 ± 4.1	30.0	25.0	37.7
Max Aneurysm Diameter (mm)					
Fusiform	107	60.3 ± 9.1	59.0	43.5	88.8
Saccular/Penetrating Ulcer	68	48.0 ± 11.9	44.8	26.2	79.8
Multiple Lesion	12	55.7 ± 7.1	55.7	44.4	71.3
Distal Neck Diameter (mm)					
Fusiform	104	31.0 ± 4.8	30.8	18.5	42.0
Saccular/Penetrating Ulcer	67	27.9 ± 4.9	27.5	17.0	42.5
Multiple Lesion	13	28.4 ± 4.5	26.4	22.0	38.0
Proximal Neck Length (mm)					
Fusiform	107	82.4 ± 50.9	78.0	12.9	234.0
Saccular/Penetrating Ulcer	67	76.2 ± 56.0	70.0	10.0	214.0
Multiple Lesion	13	79.9 ± 42.2	78.9	18.0	149.0
Aneurysm Length (mm)					
Fusiform	101	145.7 ± 71.6	157.9	30.0	297.5
Saccular/Penetrating Ulcer	66	86.8 ± 63.6	63.0	8.0	258.9
Multiple Lesion	13	107.7 ± 49.5	99.0	34.0	186.0
Distal Neck Length (mm)					
Fusiform	104	74.1 ± 51.9	62.2	10.9	225.0
Saccular/Penetrating Ulcer	67	114.5 ± 71.3	105.0	9.0	255.0
Multiple Lesion	13	90.7 ± 60.7	66.7	11.9	180.8
Right External Iliac Min Diameter (mm)					
Fusiform	71	6.5 ± 1.6	6.3	3.5	11.0
Saccular/Penetrating Ulcer	43	6.7 ± 1.5	6.5	2.9	9.7
Multiple Lesion	8	5.5 ± 1.5	5.4	4.0	7.9
Left External Iliac Min Diameter (mm)					
Fusiform	71	6.7 ± 1.5	6.5	4.0	10.9
Saccular/Penetrating Ulcer	45	6.5 ± 1.5	6.5	3.3	9.6
Multiple Lesion	8	5.8 ± 1.5	6.1	3.4	8.0
1- Denominators are n specified from readable scans.					

Table 32: Baseline Vessel Shape by Lesion Type (Core Lab Reported1) – VALOR Test Group Only

Vessel Shape	Fusiform % (m/n)	Saccular/Penetrating Ulcer % (m/n)	Multiple Lesion % (m/n)
Proximal Neck Shape			
Parallel	14.0% (15/107)	41.8% (28/67)	30.8% (4/13)
Funnel	22.4% (24/107)	22.4% (15/67)	23.1% (3/13)
Inverted Funnel	63.6% (68/107)	35.8% (24/67)	46.2% (6/13)
Distal Neck Shape			
Parallel	27.9% (29/104)	49.3% (33/67)	46.2% (6/13)
Funnel	54.8% (57/104)	37.3% (25/67)	38.5% (5/13)
Inverted Funnel	17.3% (18/104)	13.4% (9/67)	15.4% (2/13)
1- Denominators are n specified for readable scans			

Primary and Secondary Safety and Effectiveness Endpoint Analysis by Lesion Type

Table 33: Primary Safety Endpoint: All Cause Mortality by Lesion Type – VALOR Test Group Only

Lesion Type	% (m/n) [95% CI][1]
Fusiform	15.6% (17/109) [9.4%-23.8%]
Saccular/Penetrating Ulcer	15.7% (11/70) [8.1%-26.4%]
Multiple Lesion	23.1% (3/13) [5.0%-53.8%]
1 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.	

Table 34: Primary Effectiveness Endpoint: Successful Aneurysm Treatment by Lesion Type – VALOR Test Group Only

Lesion Type	% (m/n) [95% CI][1]
Fusiform	89.0% (65/73) [79.5%-95.1%]
Saccular/Penetrating Ulcer	88.2% (45/51) [76.1%-95.6%]
Multiple Lesion	100.0% (6/6) [54.1%-100.0%]
1 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.	

Table 35: Summary of Secondary Endpoints by Lesion Type – VALOR Test Group Only

Secondary Endpoints	Fusiform % (m/n) [95% CI][1]	Saccular / Penetrating Ulcer % (m/n) [95% CI][1]	Multiple Lesion % (m/n) [95% CI][1]
Successful deployment and delivery of the stent graft @ Implant	99.1% (111/112) [95.1%-100.0%]	100.0% (70/70) [94.9%-100.0%]	100.0% (13/13) [75.3%-100.0%]
"All-cause" Mortality within 30 Days	0.0% (0/112) [0.0%-3.2%]	5.7% (4/70) [1.6%-14.0%]	0.0% (0/13) [0.0%-24.7%]
Aneurysm-related death within 12 months	0.9% (1/109) [0.0%-5.0%]	7.1% (5/70) [2.4%-15.9%]	0.0% (0/13) [0.0%-24.7%]

Secondary Endpoints	Fusiform % (m/n) [95% CI][1]	Saccular / Penetrating Ulcer % (m/n) [95% CI][1]	Multiple Lesion % (m/n) [95% CI][1]
Paraplegia at 30 days	0.0% (0/112) [0.0%-3.2%]	2.9% (2/70) [0.3%-9.9%]	7.7% (1/13) [0.2%-36.0%]
Paraparesis at 30 days	9.8% (11/112) [5.0%-16.9%]	2.9% (2/70) [0.3%-9.9%]	7.7% (1/13) [0.2%-36.0%]
Secondary endovascular procedure due to endolcak within 30 days post-implantation	0% (0/111) [0.0%-3.3%]	0% (0/70) [0.0%-5.1%]	0% (0/13) [0.0%-24.7%]
Secondary endovascular procedure due to endoleak between 31 days and 12 months post-implantation	8.4% (9/107) [3.9%-15.4%]	4.5% (3/66) [0.9%-12.7%]	0% (0/13) [0.0%-24.7%]
One or more MAEs within 30 days post-implantation	46.4% (52/112) [37.0%-56.1%]	35.7% (25/70) [24.6%-48.1%]	23.1% (3/13) [5.0%-53.8%]
One or more MAEs within 12 months post-implantation	57.8% (63/109) [48.0%-67.2%]	48.6% (34/70) [36.4%-60.8%]	46.2% (6/13) [19.2%-74.9%]
One or more serious MAE within 30 days post-implantation	34.8% (39/112) [26.1%-44.4%]	24.3% (17/70) [14.8%-36.0%]	23.1% (3/13) [5.0%-53.8%]
One or more serious MAE within 12 months post-implantation	46.8% (51/109) [37.2%-56.6%]	37.1% (26/70) [25.9%-49.5%]	38.5% (5/13) [13.9%-68.4%]
Conversion to open surgical repair within 12 months post-implantation	0.0% (0/109) [0.0%-3.3%]	0.0% (0/70) [0.0%-5.1%]	7.7% (1/13) [0.2%-36.0%]
Migration of stent graft >10 mm between 1 and 12 months	5.6% (3/54) [1.2%-15.4%]	2.3% (1/44) [0.1%-12.0%]	0.0% (0/5) [0.0%-52.2%]
Loss of patency of the stent graft at 12-month visit	0% (0/60) [0.0%-6.0%]	0% (0/42) [0.0%-8.4%]	0% (0/5) [0.0%-52.2%]
Aneurysm rupture within 12 months post-implantation	0.9% (1/109) [0.0%-5.0%]	0.0% (0/70) [0.0%-5.1%]	0.0% (0/13) [0.0%-24.7%]
Endoleaks at 12-month visit	13.2% (9/68) [6.2%-23.6%]	12.2% (6/49) [4.6%-24.8%]	0.0% (0/6) [0.0%-45.9%]
1 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.			

Table 36: Persistent Paraplegia/Paraparesis at 12 Months or last Follow-up by Lesion Type – VALOR Test Group Only

Safety Endpoint	Fusiform % (m/n) [95% CI][1]	Saccular / Penetrating Ulcer % (m/n) [95% CI][1]	Multiple Lesion % (m/n) [95% CI][1]
Paraplegia (at 12 months or last follow-up)	0.9% (1/109) [0.0%-5.0%]	2.9% (2/70) [0.3%-9.9%]	7.7% (1/13) [0.2%-36.0%]
Paraparesis (at 12 months or last follow-up)	5.5% (6/109) [2.0%-11.6%]	0.0% (0/70) [0.0%-5.1%]	0.0% (0/13) [0.0%-24.7%]
1 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.			

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A. Long-Term Results of Primary Clinical Study

Overview of Long-Term Data and Follow-Up

Subjects in the VALOR Test Group are to be followed through five years as a condition of approval. All the VALOR Test Group subjects have been followed to a minimum of 2 years unless they terminated and this data is presented below. Data for all VALOR Test Group subjects will continue to be collected up to 5-years. At the 2 year follow-up interval, 139 subjects were eligible for clinical and imaging follow-up. Of these, 71.2% (99/139) had clinical follow-up and CT imaging was performed on 68.3% (95/139) subjects. Detailed patient accounting and follow-up is provided in Table 37.

Table 37: 2-Year Patient and Imaging Accountability, VALOR Test Group

Interval	Patient follow-up			Patients with imaging performed at time interval (site reported)			Patients with adequate imaging to assess the parameter				Patient events occurring before next visit					
	Eligible	Clinical Follow-up	Imaging Follow-up	CT/MR Imaging	KUB Imaging	Additional Imaging modalities	Aneurysm size increase	Endoleak	Migration	Integrity	Technical Failure	Conversion to Surgery	Death	Withdrawal	Lost to Follow-up	Not Due for Next Visit
Originally Enrolled	195										1					
Events before 2-year visit[1]												2	43	8	2	0
Events at 2-year visit (Day 700-845)	139	99	95	95	81	0	91	92	92	81						

1 - "Events before 2 year visit" includes all events in the 1-year Patient and Imaging Accountability (Table 6) and additional events that occurred after the 1 year visit but prior to the 2-year visit.

Key Long-Term Safety and Effectiveness Outcomes

Available data up to 2-year follow-up period continues to support the safety and effectiveness of the Talent™ Thoracic Stent Graft within the indicated patient population. Refer to Tables 38 through 43 and Figures 11 through 14 for further information.

Table 38: Summary of Primary Safety Endpoint at 2-Years – VALOR Test Group

Primary Endpoint – "All cause" mortality	% (m/n) [95% CI]
At 24-month visit	22.6% (42/186)[1] [16.8%-29.3%][2]

1 - Evaluable subjects include those who died within 730 days post procedure and those on study > 700 days.
2 - Confidence level was not adjusted for multiplicity. Confidence interval for the percentage was calculated by the exact (binomial) method.

Figure 11: - Kaplan-Meier Estimate of VALOR Test Group – Summary of Primary Safety Endpoint at 2 Years

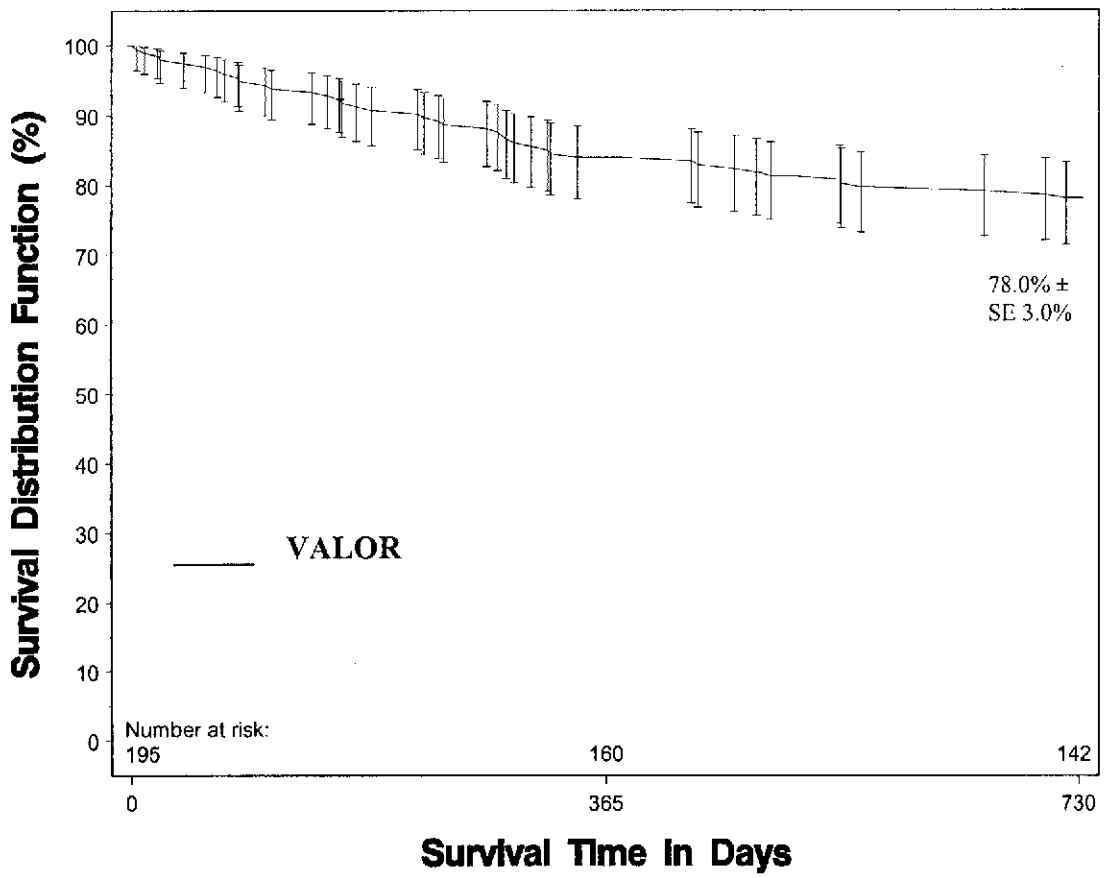


Table 39: Details of Kaplan-Meier Estimate of VALOR Test Group – Summary of Primary Safety Endpoint at 2 Years

	VALOR Test Group			
	Treatment – to 30 days	31 days to 182 days	183 days to 365 days	366 days to 730 days
No. at Risk	195	190	176	160
No. of Events	4	13	14	11
No. Censored	1	1	2	7
Kaplan-Meier Estimate	0.980	0.912	0.839	0.780

Table 40: Additional Endpoints at 2 Years – VALOR Test Group

Intervention	> 365 days % (m/n)
Additional Endovascular Repair[1]	1.9% (3/157)[2]
Conversion to Open Surgical Repair[1]	0.6% (1/157)[3]
Aneurysm Rupture[1]	0.0% (0/157)

1- Evaluable subjects includes those who experienced an event between 366 and 730 days post procedure and those subjects alive and on study > 365 days.

2 - The 3 subjects who received an additional endovascular procedure post-365 days are characterized as follows:

- One subject was detected with an endoleak at day 354 and underwent a second procedure on day 379. A proximal main and two distal extension sections were placed to correct a Type I endoleak (distal). No other serious events are reported for this patient.
- One patient was detected with an endoleak at day 352 and underwent a second procedure on day 420. A distal extension was placed to correct a Type I (distal) endoleak. An additional endoleak was reported for this patient on day 443, which was resolved via a coil embolization procedure on day 457. This patient subsequently expired due to emphysema at day 887. No other endoleak-related events are reported for this patient.
- One patient was detected with an endoleak at day 644 and underwent a second procedure on day 672. Two proximal main devices were placed to correct a Type I (proximal) endoleak. No other serious events are reported for this patient.

3 - One patient underwent a surgical conversion on day 497 to resect the thoracic aorta to correct persistent distal aneurysmal expansion noted, without evidence of endoleak. Surgical repair was recommended due to an inadequate neck length above the celiac artery. No other endoleak-related events are reported for this patient.

Figure 12: Kaplan-Meier Estimate of 2-Year Freedom from Aneurysm Rupture, VALOR Test Group

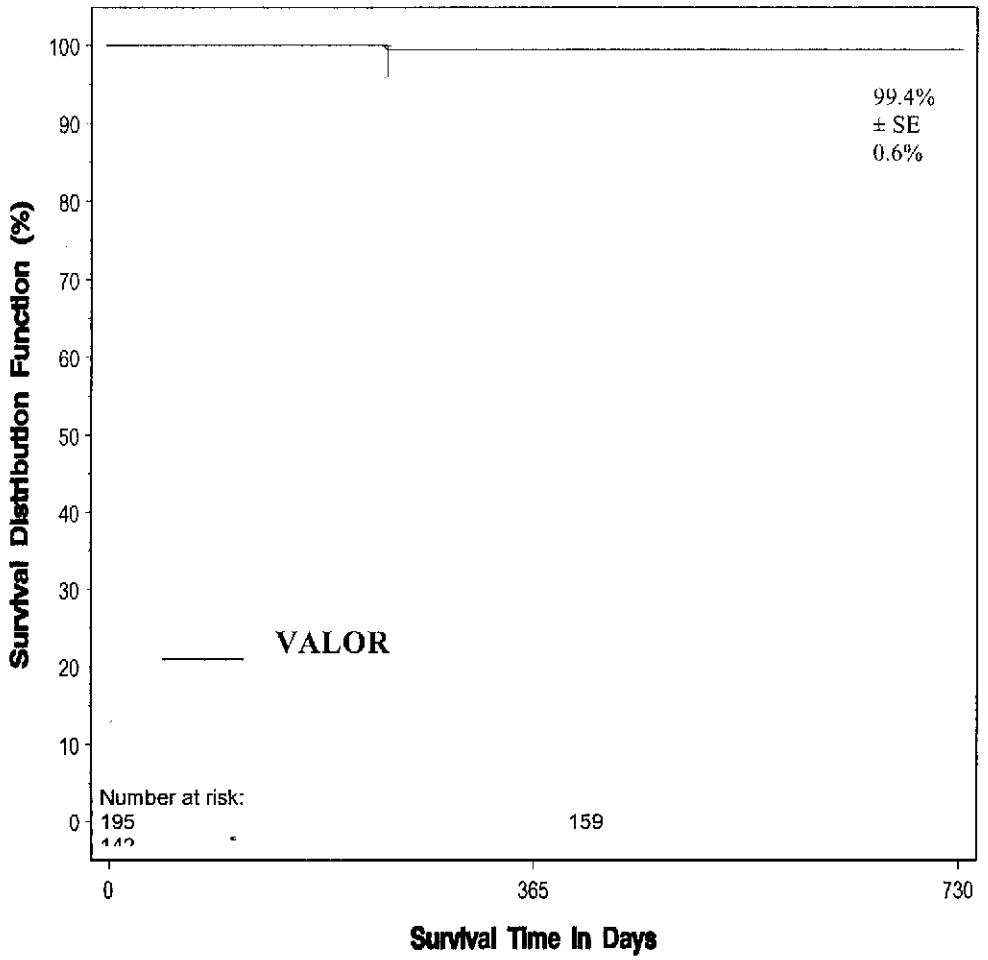


Table 41: Details of Kaplan-Meier Estimate of 2-Year Freedom from Aneurysm Rupture, VALOR Test Group

	VALOR Test Group			
	Treatment to 30 days	31 days to 182 days	183 days to 365 days	366 days to 730 days
No. at Risk	195	190	175	159
No. of Events	0	0	1	0
No. Censored	5	15	15	17
Kaplan-Meier Estimate	1.000	1.000	0.994	0.994

Figure 13: Kaplan-Meier Estimate of 2-Year Freedom from Secondary Procedure, VALOR Test Group

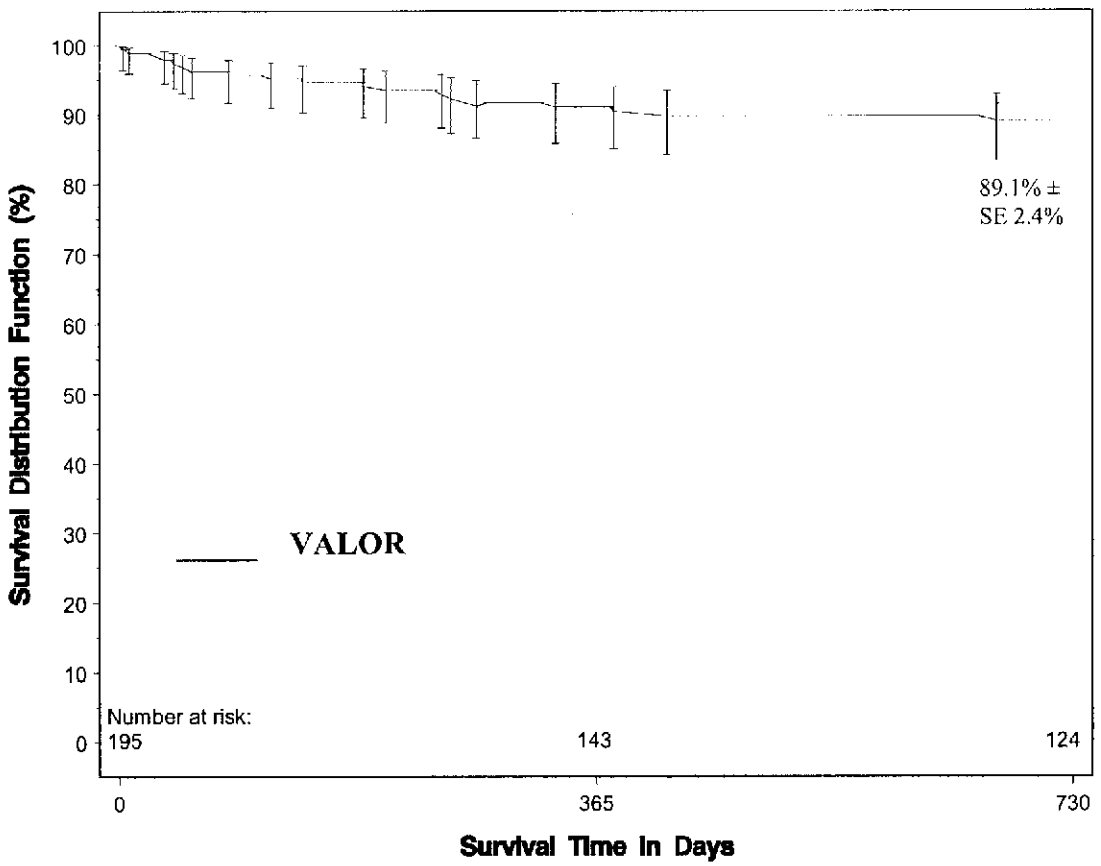


Table 42: Details of Kaplan-Meier Estimate of 2-Year Freedom from Secondary Procedure, VALOR Test Group

	VALOR Test Group			
	Treatment to 30 days	31 days to 182 days	183 days to 365 days	366 days to 730 days
No. at Risk	195	187	164	143
No. of Events	2	8	6	3
No. Censored	6	15	15	16
Kaplan-Meier Estimate	0.990	0.946	0.917	0.891

Figure 14: Kaplan-Meier Estimate of 2-Year Freedom from Surgical Conversion, VALOR Test Group

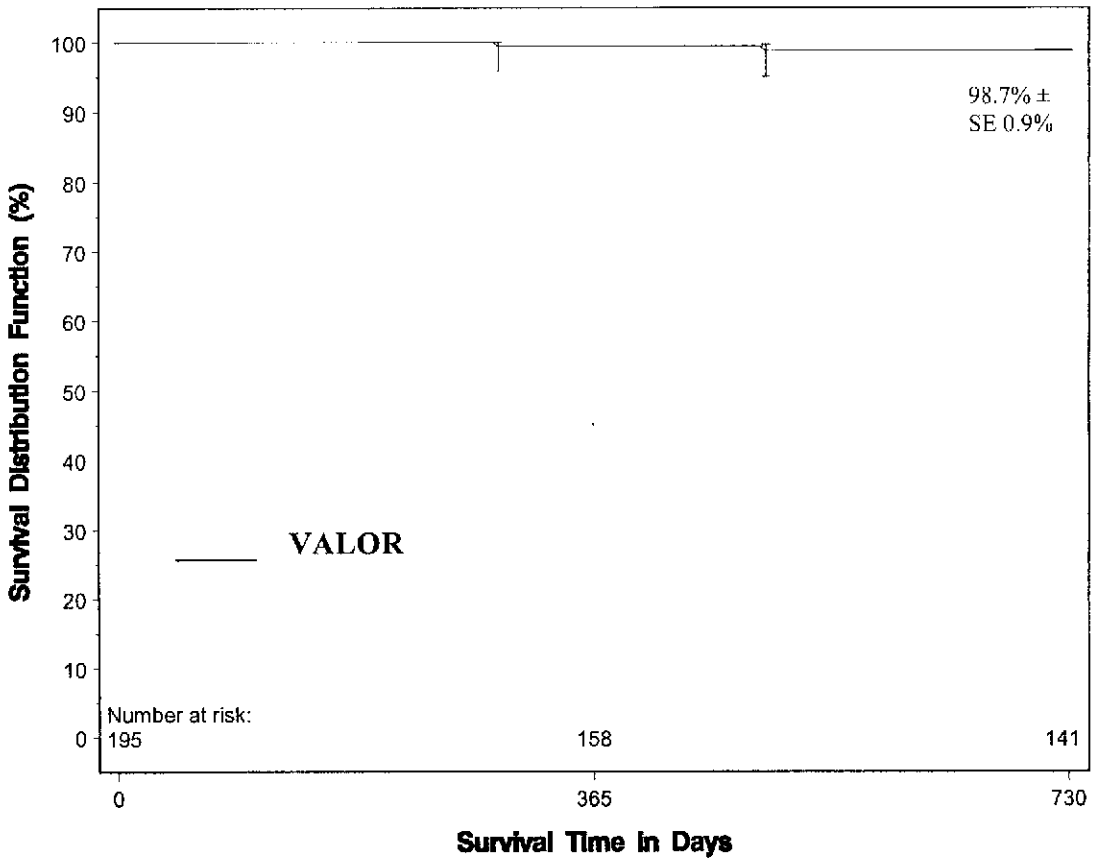


Table 43: Kaplan-Meier Estimate of 2-Year Freedom from Surgical Conversion, VALOR Test Group

	VALOR Test Group			
	Treatment to 30 days	31 days to 182 days	183 days to 365 days	366 days to 730 days
No. at Risk	195	190	175	158
No. of Events	0	0	1	1
No. Censored	5	15	16	16
Kaplan-Meier Estimate	1.000	1.000	0.994	0.987

B. Other Observed Events

Medtronic also provided additional information from different clinical sources for the following types of events:

- **Misaligned opening** occurs when, during deployment, the proximal stent graft structure unfolds (opens) in an alignment that is not parallel to the wall of the aorta and may be correctable through appropriate deployment technique. In some instances, misaligned opening may result in misaligned stent graft deployment.

- **Misaligned deployment** can occur when the proximal stent apices of a deployed stent graft remain significantly non-parallel to the wall of the aorta after deployment has been completed. Misaligned deployment may occur when an operator fails to (or cannot) retract the stent graft in order to correct an asymmetry opening or when a partially opened stent graft is pushed proximally. Potential clinical sequelae of misaligned deployment range from negligible to significant and may present either acutely or chronically.
    - Severity 1: No clinical impact- unresolved mild asymmetry or stent apex protrusion into the aortic wall without clinical impact, including no evidence of endoleak, graft narrowing/occlusion or perforation.
    - Severity 2: Clinical impact- unresolved asymmetry or stent apex protrusion into the aortic wall with clinical impact, including evidence of endoleak or luminal narrowing of the endograft.

- **Aortic perforation** is defined as full-thickness penetration of the wall of the aorta or the wall of the aneurysm by components of the deployed or partially deployed device with evidence of contrast extravasation outside of the aortic wall. Aortic perforation may occur due to the advancement of a partially deployed graft, inflation of a balloon over the uncovered portion of the graft, failure to implant the proximal and distal springs of the stent graft in healthy tissue or when the Talent™ Thoracic Stent Graft is used in conjunction with other surgical grafts.

- **Type A dissection** is defined as partial disruption of the aortic intimal layer with extrusion of blood into the medial layer causing separation of the natural vessel layers. Type A dissection may occur due to implantation in the presence of dissections, inflation of a balloon over the uncovered portion of a graft; failure to place the stent graft in an adequate landing zone comprised of healthy tissue; or, excessive wire/catheter manipulations in the ascending and transverse arch. Type A dissections have occurred with all endografts, as well as in open surgery or even in diagnostic angiography alone. There are also reports of spontaneous, Type A dissections in patients receiving only medical management.[3,4,5]

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[3] Di Cesare E et al, MRI postoperative monitoring in patients surgically treated for aortic dissection, Magn Reson Imaging. 1996;14(10):1149-56.

[4] Elefteriades, J.A., Natural History of Thoracic Aortic Aneurysms: Indications for Surgery, and Surgical Versus Nonsurgical Risks, Ann. Thorac. Surg, 2002, pp S1877-1880.

[5] Fattori R, Lovato L, et. al.. Extension of dissection in stent-graft treatment of type B aortic dissection: lessons learned from endovascular experience. J Endovasc Ther. 2005 Jun;12(3):306-11.

Table 44 summarizes the number of these events reported in the first 10 years of clinical experience with the Talent™ Thoracic Stent Graft System within the U.S. (investigational) and OUS (commercial).

Table 44: Number of Adjudicated Events by Study/Cohort

Distribution Cohort	Misaligned Opening / Deployment Events	Aortic Perforation (Target Lesion) Events	Retrograde Dissection Events
U.S. Feasibility Studies	--	--	--
U.S. VALOR Studies			
Test[1]	--	--	Test Group – 3
High Risk	--	--	High Risk Group - 1
Registry	--	--	--
U.S. Emergency / Compassionate Use	--	--	1
U.S. S-I IDE Studies[2]	3	--	5
OUS Commercial Sales	7[3]	8	29[4]
Total	10	8	39

1 – The test group is the same VALOR Test Group discussed in Section X above.
2 - The Talent™ Thoracic Stent Graft is the subject of 7 U.S. Sponsor-Investigator IDEs.
3 - Includes one (1) event of misaligned opening and six (6) events of misaligned deployment.
4 - The OUS indication for use includes treatment of patients with chronic type-B dissections.

An independent physician review committee concurred that the four event types are generally related to off-label and/or inappropriate device usage and can be mitigated through training, proper deployment technique, proper patient selection, imaging, case planning, and adequate labeling.

XII. PANEL MEETING RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The results of the preclinical testing (i.e., biocompatibility, product testing, animal studies, packaging, shelf life testing, and sterilization) were adequate and raised no safety issues.

The safety data from the VALOR pivotal dataset showed that the 12-month All-Cause Mortality for the treatment patients (16.1%) met the pre-specified performance goal of 29.8% taken from the literature control. The VALOR Test Group also experienced a lower rate of All-Cause Mortality at 30 days when compared to the Retrospective Open Surgery Group (2% vs. 8%). The rate of MAEs at 30 days was also less in the treatment group as compared to the Retrospective Open Surgical Control Group (41.0% vs. 84.4%). All clinical utility measures were reduced in the VALOR Test Group compared to the Retrospective Open Surgery Group.

Effectiveness was evaluated as Successful Aneurysm Treatment at 12 months. Successful aneurysm treatment was defined as no aneurysm growth greater than 5mm and absence of a Type I endoleak as assessed by the Core Lab. The rate of successful aneurysm treatment at 12 months for the Talent™ Thoracic Stent Graft was 89.2% (confidence interval of 82.6-94.0%), meeting the pre-specified performance goal of 80%. There was one conversion to open repair and one aneurysm rupture in the endovascular treatment group within 12 months. Clinical data beyond 12 months continue to support device safety and effectiveness, and follow-up remains on-going through a post-approval study.

Overall, the data in this application support the reasonable assurance of safety and effectiveness of the Talent™ Thoracic Stent Graft System when used in accordance with the indications for use.

XIV. CDRH DECISION

CDRH issued an approval order on June 5, 2008. The final conditions of approval cited in the approval order are described below.

- Medtronic must provide a clinical update to physician users at least annually. At a minimum, this update will include, for their pivotal study cohort and their post-approval study cohort, a summary of the number of patients for whom data are available, with the rates of aneurysm rupture, secondary endovascular procedures, conversion to surgical repair, aneurysm-related mortality, major adverse events, endoleak, aneurysm enlargement, prosthesis migration, patency, misaligned deployment, aortic perforation and retrograde dissection. Reports of losses of device integrity, reasons for conversion and causes of aneurysm-related death and rupture are to be described. A summary of any explant analysis findings are to be included. Additional relevant information from commercial experience within and outside of the U.S. is also to be included. The clinical updates for physician users and the information supporting the updates must be provided in supplements to their PMA.

- Medtronic must perform a post-approval study for the Talent™ Thoracic Stent Graft System to evaluate the longer-term safety and effectiveness of the Talent™ Thoracic Stent Graft through five years of implantation. The primary endpoint for this study is freedom from aneurysm-related mortality at 5 years. Aneurysm-related mortality is defined as:

  > Death from rupture of the thoracic aortic aneurysm or from any procedure intended to treat the Descending Thoracic Aneurysm (DTA) (fusiform aneurysms and saccular aneurysms/penetrating ulcers) as determined by the independent clinical events committee. If a death occurred within one month of any procedure intended to treat the DTA, then it is presumed to be aneurysm related, unless there was evidence to the contrary.

  This study is expected to include 451 patients, 195 endovascular patients from the original pivotal study cohort, as well as enrollment of an additional 256 patients at a minimum of 15 investigational sites. At 1 month, 12 months, and, at each annual visit, a contrast enhanced CT scan, chest x-ray and physical examination will be conducted. All data will be entered into a database, analyzed, and submitted in post-approval reports to the FDA, and a final

report will be submitted after completion of the follow-up and analysis. This follow-up plan will allow an evaluation of aneurysm-related mortality, major adverse events, migration, patency, endoleaks, device integrity, aneurysm enlargement, aneurysm rupture, secondary endovascular procedures and conversion to open surgical repair over time. This post-approval study will also include additional analyses for misaligned deployment, aortic perforation, and retrograde dissection. Upon completion of this post-approval study, Medtronic must provide a supplement with revised labeling that reflects the study findings.

- Medtronic must perform an evaluation to better understand the overall outcomes in females and non-Caucasians undergoing endovascular aneurysm repair (EVAR) with the Talent™ Thoracic Stent Graft System. This evaluation will include a subset evaluation of the females and non-Caucasians enrolled in the post-approval study described in item 2 above, as well as a summary of the current literature research results of females and non-Caucasians having undergone EVAR. This evaluation is to include descriptive statistics to summarize literature-derived outcomes in patients with the EVAR therapy, literature-derived Talent™ Thoracic Stent Graft-specific outcomes, and post-approval study outcomes in female and non-Caucasians populations. Findings of this evaluation must be provided with each regular post-approval study report update until the completion of the post-approval study described in item 2 above.

- Medtronic must implement a training program, as outlined in the PMA, which includes a subset analysis examining the skills of new practitioners in the use of the Talent™ Thoracic Stent Graft System. This evaluation will include a subset of the additional 256 patients enrolled in the post-approval study described in item 2 above. Medtronic will compare 30-day results, including death, conversion to surgery, delivery and deployment success, misaligned deployment, aortic perforation, type A retrograde dissection, secondary procedures, and stroke, from novice implanters (physicians with ≤ 5 cases) to 30-day results from the same implanters (> 5 cases) for a total of 10 implants. Findings of this evaluation must be provided with the post-approval study report updates.

The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling.

Hazards to Health from Use of Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Post Approval Requirements and Restrictions: See approval order.