

# Summary of Safety and Effectiveness Data (SSED)

## I. GENERAL INFORMATION

Device Generic Name:	Thoracic Endovascular Graft
Device Trade Name:	Zenith TX2 <sup>®</sup> TAA Endovascular Graft
Applicant Name and Address:	William Cook Europe, ApS Sandet 6, DK 4632 Bjaeverskov, Denmark
Premarket Approval Application (PMA) Number:	P070016
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	May 21, 2008
Expedited:	Not applicable

## II. INDICATIONS FOR USE

The Zenith TX2<sup>®</sup> TAA Endovascular Graft with the H&L-B One-Shot<sup>™</sup> Introduction System is indicated for the endovascular treatment of patients with aneurysms or ulcers of the descending thoracic aorta having vascular morphology suitable for endovascular repair, including:

- Adequate iliac/femoral access compatible with the required introduction systems,
- Non-aneurysmal aortic segments (fixation sites) proximal and distal to the aneurysm or ulcer:
  - with a length of at least 25 mm, and
  - with a diameter measured outer wall to outer wall of no greater than 38 mm and no less than 24 mm.

## III. CONTRAINDICATIONS

The Zenith TX2 TAA Endovascular Graft with the H&L-B One-Shot Introduction System is contraindicated in:

- Patients with known sensitivities or allergies to stainless steel, polyester, solder (tin, silver), polypropylene, nitinol, or gold.
- Patients with a systemic infection which may be at increased risk of endovascular graft infection.

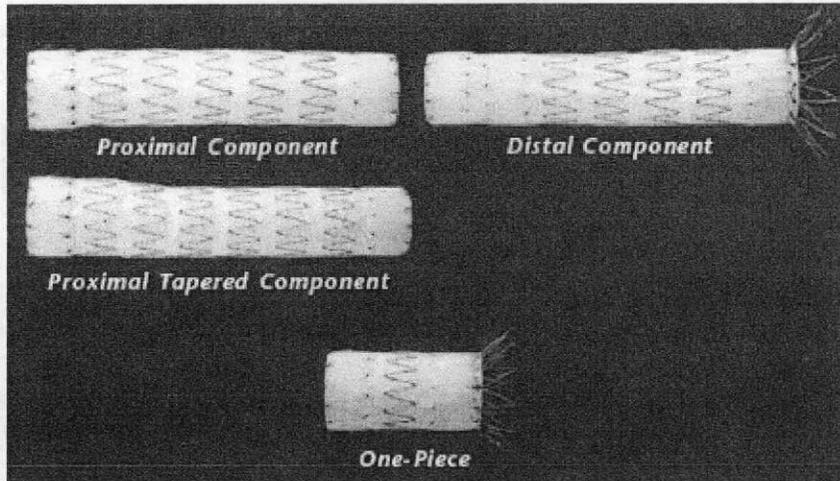
## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Zenith TX2<sup>®</sup> TAA Endovascular Graft labeling (Instructions for Use).

V. **DEVICE DESCRIPTION**

**Main Body Component Description**

The Zenith TX2<sup>®</sup> TAA Endovascular Graft is a two- or one-piece cylindrical endovascular graft. The two-piece system consists of a proximal main body component and overlapping distal main body component. The one-piece system may consist of either a one-piece main body component or a proximal main body component (without use of a distal main body component). The proximal main body components can be either tapered (by 4 mm) or non-tapered. All main body components are shown in Figure 1.



**Figure 1. Zenith TX2<sup>®</sup> TAA Endovascular Graft main body components.**

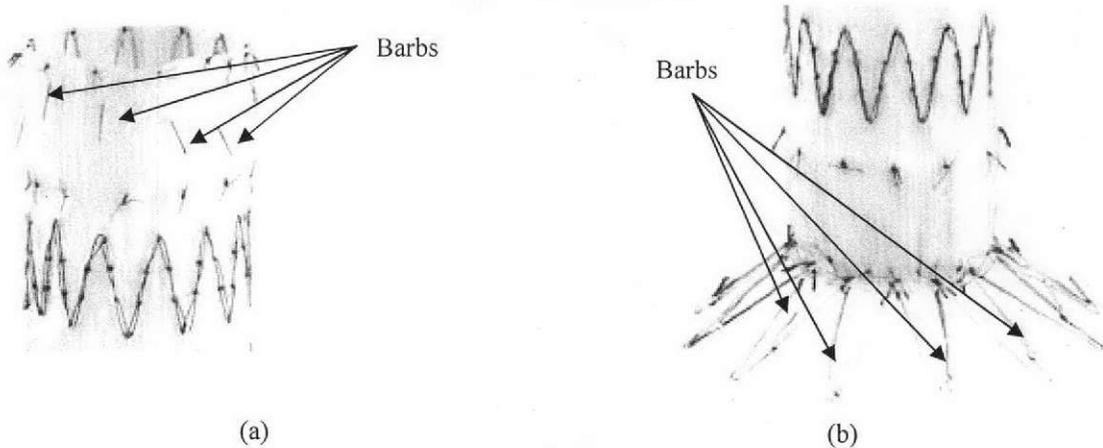
As listed in Table 1, the Zenith TX2<sup>®</sup> TAA Endovascular Graft main body components are available in a variety of standard stock sizes.

**Table 1. Zenith TX2<sup>®</sup> TAA Endovascular Graft main body components by diameter**

Graft diameter (mm)	Length of non-tapered proximal component (mm)	Length of tapered proximal component (mm)	Length of distal component (mm)	Length of one-piece component (mm)
28	120 / 140 / 200	n/a	127 / 147 / 207	84
30	120 / 140 / 200	n/a	127 / 147 / 207	84
32	120 / 140 / 200	160 / 200	127 / 147 / 207	84
34	127 / 152 / 202	157 / 197	136 / 186	81
36	127 / 152 / 202	157 / 197	136 / 186	81
38	127 / 152 / 202	152 / 202	136 / 186	81
40	108 / 135 / 162 / 216	158 / 208	144 / 198	85
42	108 / 135 / 162 / 216	158 / 208	144 / 198	85

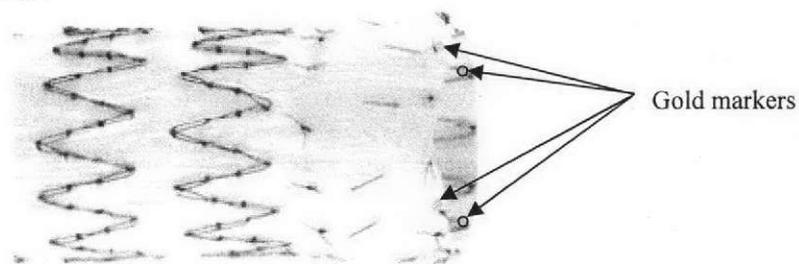
The stent-grafts are constructed of full-thickness woven polyester fabric sewn to self-expanding stainless steel Cook-Z<sup>®</sup> stents with braided polyester and monofilament polypropylene sutures. The Zenith TX2<sup>®</sup> TAA Endovascular Graft is fully stented to provide stability and the expansile force necessary to open the lumen of the graft during deployment. Additionally, the Cook-Z<sup>®</sup> stents provide the necessary attachment and seal of the graft to the vessel wall. For added fixation, the covered stent at the proximal end of the proximal main body component

(tapered and non-tapered) and one-piece main body component contains barbs placed at a 2 mm stagger, which protrude through the graft material (Figure 2a). The bare stent at the distal end of the distal main body component and one-piece main body component also contains barbs (Figure 2b). The number of barbs per covered or uncovered stent depends on component diameter, such that barbed stents on 28 to 40 mm diameter components contain 12 barbs and barbed stents on 42 mm diameter components contain 14 barbs.



**Figure 2. Proximal (a) and distal (b) barbed stents.**

To facilitate fluoroscopic visualization of the endovascular graft, four gold radiopaque markers are positioned on each end of every main body component. These markers are threaded on the stent wires and placed in a circumferential orientation within 1 mm of the most proximal aspect of the graft material and within 1 mm of the most distal aspect of the graft material, such as shown in Figure 3.



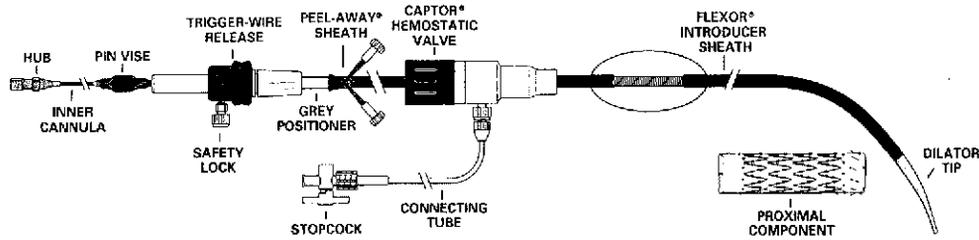
**Figure 3. Positioning of gold radiopaque markers.**

### **Main Body Component Delivery System Description**

The Zenith TX2<sup>®</sup> TAA Endovascular Graft is shipped preloaded onto the H&L-B One-Shot<sup>™</sup> Introduction System. It has a sequential deployment method with built-in features to provide continuous control of the endovascular graft throughout the deployment procedure. The H&L-B One-Shot<sup>™</sup> Introduction System enables precise positioning before deployment of its loaded component.

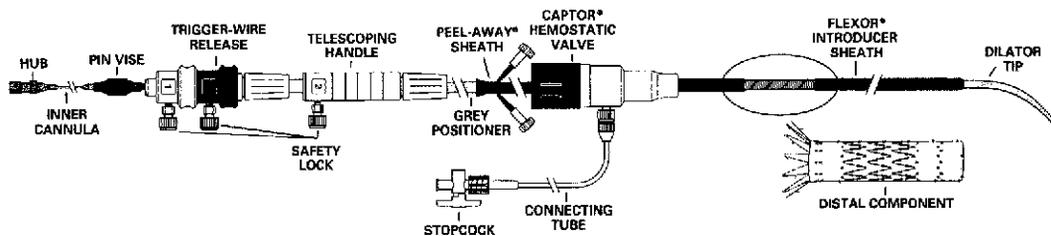
Depending on component diameter, the main body components are deployed from either a 20 Fr or 22 Fr H&L-B One-Shot<sup>™</sup> Introduction System. All 28 to 34 mm diameter components are deployed using a 20 Fr system, and all 36 to 42 mm diameter components are deployed using a 22 Fr system.

All proximal main body components are deployed from an H&L-B One-Shot™ Introduction System that utilizes a single trigger-wire release mechanism to secure the endovascular graft onto the delivery system until released by the physician. Additionally, the delivery system is pre-curved to facilitate positioning within the aortic arch. An illustration of the proximal main body component delivery system is shown in Figure 4.



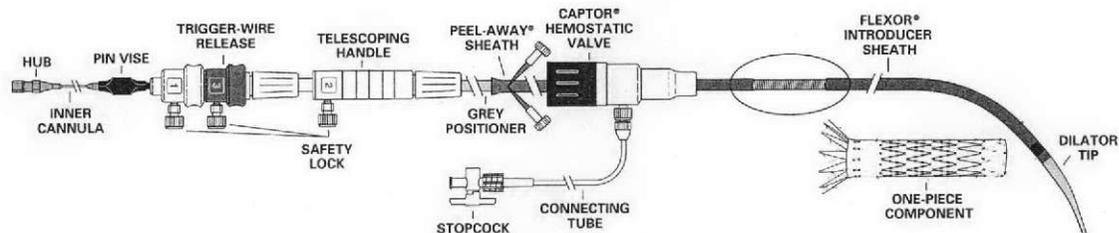
**Figure 4. Proximal main body component delivery system.**

All distal main body components are deployed from an H&L-B One-Shot™ Introduction System that utilizes a dual trigger-wire release mechanism to secure the endovascular graft onto the delivery system until released by the physician. The delivery system is straight with a pre-curved tip. An illustration of the distal main body component delivery system is shown in Figure 5.



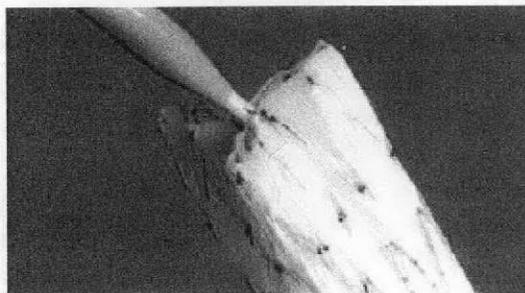
**Figure 5. Distal main body component delivery system.**

All one-piece main body components are deployed from an H&L-B One-Shot™ Introduction System that utilizes a dual trigger-wire release mechanism to secure the endovascular graft onto the delivery system until released by the physician. Additionally, the delivery system is pre-curved to facilitate positioning within the aortic arch. An illustration of the one-piece main body component delivery system is shown in Figure 6.



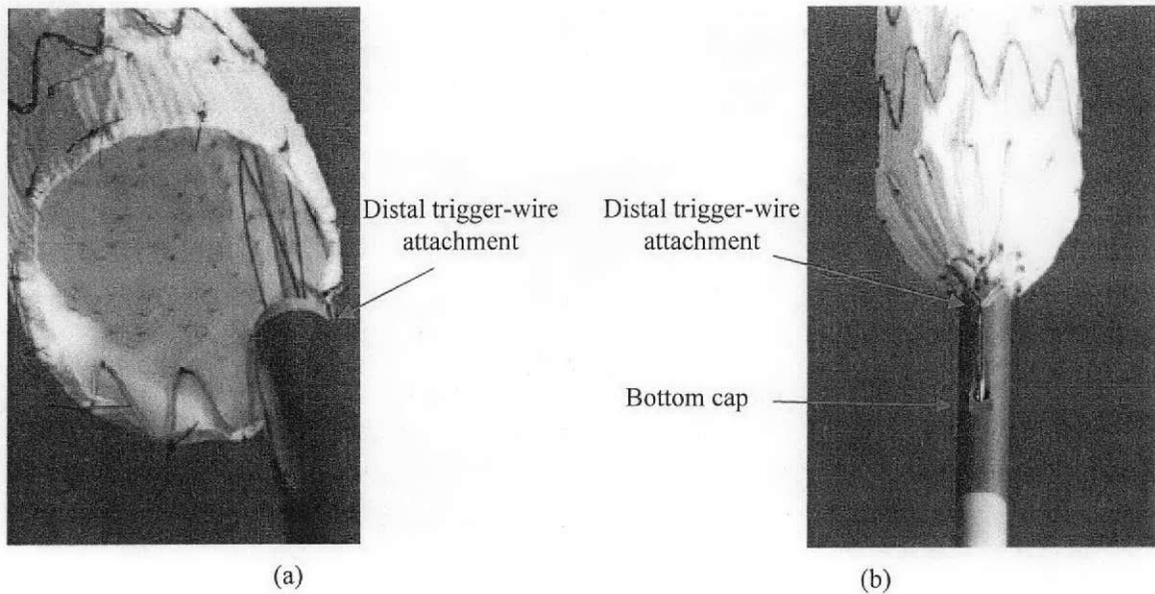
**Figure 6. One-piece main body component delivery system.**

All delivery systems are compatible with a .035 inch wire guide. For added hemostasis, the Captor™ Hemostatic Valve can be loosened or tightened for the introduction and/or removal of ancillary devices into and out of the sheath. All delivery systems feature the Flexor® introducer sheath, which resist kinking and are hydrophilically coated. Both features of the introducer sheath are intended to enhance trackability from the iliac arteries to the thoracic aorta. The hydrophilic coating, in particular, is intended to minimize access site complications. The Flexor® introducer sheath has a marker at the tip to facilitate visualization during introduction. The trigger-wire release mechanisms of the respective systems work in tandem to deliver sequential, controlled release of the Zenith TX2® TAA Endovascular Graft during deployment. Once the sheath is withdrawn, the proximal end of all main body components remain attached to their respective delivery systems with the use of three trigger-wires, which keep the proximal end of the graft in a 'tri-fold' configuration (Figure 7), thus maintaining position of the endovascular graft with respect to target anatomy by allowing for blood flow around the graft.



**Figure 7. Configuration of unsheathed proximal end constrained by trigger-wires.**

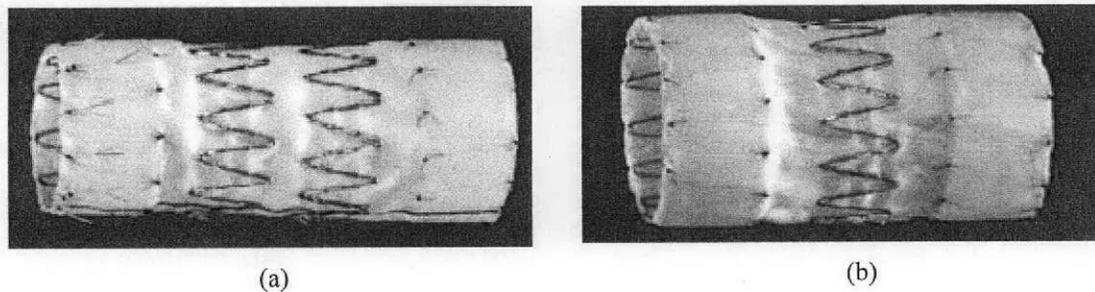
The distal end of each main body component is also attached to the delivery system by trigger-wires. As shown in Figure 8(a), the proximal main body components are attached at the distal end by a single trigger-wire. Figure 8(b) depicts the distal end attachment for the distal main body components and one-piece main body components, which utilize a bottom cap to contain the distal bare stent as well as a trigger-wire to fix the graft to the delivery system bottom cap.



**Figure 8. Distal trigger-wire attachments for proximal main body components (a) and distal main body components/one-piece main body components (b).**

**Ancillary Component Description**

Ancillary devices comprising the Zenith TX2<sup>®</sup> TAA Endovascular Graft product line consist of proximal main body extensions and distal main body extensions, as shown in Figure 9. Both the proximal and distal main body extensions can be used to provide additional length to their respective portions of the main body components. Additionally, the distal main body extension can be used to increase the overlap length between components.



**Figure 9. Proximal (a) and distal (b) main body extensions.**

As listed in Table 2, the Zenith TX2<sup>®</sup> TAA Endovascular Graft proximal and distal main body extensions are available in a variety of standard stock sizes.

**Table 2. Zenith TX2<sup>®</sup> TAA Endovascular Graft main body extensions by diameter**

Graft diameter (mm)	Length of proximal extension (mm)	Length of distal extension (mm)
28	80	80
30	80	80
32	80	80
34	77	77
36	77	77
38	77	77
40	81	81
42	81	81

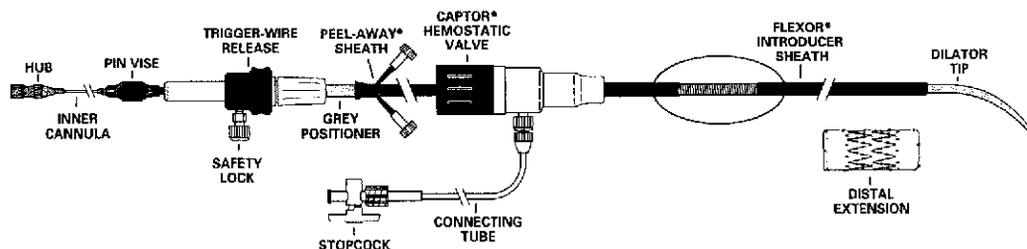
The main body extensions are constructed of the same materials as are used to construct the main body components. As with the proximal main body component and one-piece main body component, the covered stent at the proximal end of the proximal main body extension contains barbs for added fixation. The distal main body extension does not contain any barbs. Same as the main body components, the main body extensions contain four gold radiopaque markers at each end of the graft to facilitate fluoroscopic visualization.

**Ancillary Component Delivery System Description**

The Zenith TX2<sup>®</sup> TAA Endovascular Graft proximal and distal main body extensions are also shipped preloaded onto the H&L-B One-Shot<sup>™</sup> Introduction System. Same as the main body components, all 28 to 34 mm diameter main body extensions are deployed using a 20 Fr system, and all 36 to 42 mm diameter main body extensions are deployed using a 22 Fr system.

The proximal main body extension uses the same H&L-B One-Shot<sup>™</sup> Introduction System design as that used for the proximal main body components, i.e., pre-curved delivery system with a single trigger-wire release mechanism.

All distal main body extensions are deployed from an H&L-B One-Shot<sup>™</sup> Introduction System that utilizes a single trigger-wire release mechanism to secure the endovascular graft onto the delivery system until released by the physician. The delivery system is straight with a pre-curved tip. An illustration of the distal main body extension delivery system is shown in Figure 10.



**Figure 10. Distal main body extension delivery system.**

As with the main body components, all delivery systems are compatible with a .035 inch wire guide, feature the Captor™ Hemostatic Valve, and incorporate the Flexor® introducer sheath. Additionally, the proximal and distal ends of both proximal and distal main body extensions remain tethered to the delivery in the same fashion as the proximal main body components.

## **VI. ALTERNATIVE PRACTICES AND PROCEDURES**

The traditional standard of care for treatment of thoracic aortic aneurysms or ulcers is surgical implantation of a synthetic graft within the diseased vessel, use of another commercially-available endovascular graft for the treatment of thoracic aortic aneurysms, 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**

The Zenith TX2® TAA Endovascular Graft with the H&L-B One-Shot™ Introduction System is currently available throughout much of the world following approval by the Therapeutic Goods Administration in 2002 and CE marking in 2004. The Zenith TX2® TAA Endovascular Graft has not been withdrawn from any market for reasons related to safety or effectiveness.

## **VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Adverse events that may occur and/or require intervention include, but are not limited to:

- Amputation
- Anesthetic complications and subsequent attendant problems (e.g., aspiration)
- Aneurysm enlargement
- Aneurysm rupture and death
- Aortic damage, including perforation, dissection, bleeding, rupture and death
- Aorto-bronchial fistula
- Aorto-esophageal fistula
- Arterial or venous thrombosis and/or pseudoaneurysm
- Arteriovenous fistula
- Bleeding, hematoma, or coagulopathy
- Bowel complications (e.g., ileus, transient ischemia, infarction, necrosis)
- Cardiac complications and subsequent attendant problems (e.g., arrhythmia, tamponade, myocardial infarction, congestive heart failure, hypotension, hypertension)
- Claudication (e.g., buttock, lower limb)
- Compartment Syndrome
- Death
- Edema
- Embolization (micro and macro) with transient or permanent ischemia or infarction
- Endoleak
- Endoprosthesis: improper component placement; incomplete component deployment; component migration and/or separation; suture break; occlusion; infection; stent fracture; graft material wear; dilatation; erosion; puncture; perigraft flow; barb separation and corrosion
- Femoral neuropathy

- Fever and localized inflammation
- Genitourinary complications and subsequent attendant problems (e.g., ischemia, erosion, fistula, urinary incontinence, hematuria, infection)
- Hepatic failure
- Impotence
- Infection of the aneurysm, device or access site, including abscess formation, transient fever and pain
- Lymphatic complications and subsequent attendant problems (e.g., lymph fistula, lymphocele)
- Local or systemic neurologic complications and subsequent attendant problems (e.g., stroke, transient ischemic attack, paraplegia, paraparesis/spinal cord shock, paralysis)
- Occlusion of device or native vessel
- Pulmonary Embolism
- Pulmonary/respiratory complications and subsequent attendant problems (e.g., pneumonia, respiratory failure, prolonged intubation)
- Renal complications and subsequent attendant problems (e.g., artery occlusion, contrast toxicity, insufficiency, failure)
- Surgical conversion to open repair
- Vascular access site complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula
- Vascular spasm or vascular trauma (e.g., ilio-femoral vessel dissection, bleeding, rupture, death)
- Wound complications and subsequent attendant problems (e.g., dehiscence, infection).

## **IX. SUMMARY OF NON-CLINICAL STUDIES**

### **A. Biocompatibility**

Biocompatibility of the Zenith TX2<sup>®</sup> TAA Endovascular Graft implant was assessed by testing specified in the ISO standard 10993-1 *Biological Evaluation of Medical Devices* including cytotoxicity, sensitization, skin irritation or intracutaneous reactivity, acute systemic toxicity, pyrogenicity, genotoxicity, and mutagenicity, hemocompatibility (hemolysis, coagulation, and complement activation), subchronic toxicity, and reaction toward implantation (4-week, 12-week, and 16-week muscle implant). Testing for carcinogenicity was considered unnecessary given the significant history of long-term biocompatibility of these implantable materials. Neither reproductive/developmental nor biodegradation testing were suggested by the standard for implantable blood-contacting devices.

Likewise, the biocompatibility of the H&L-B One-Shot<sup>™</sup> Introduction System was assessed by testing specified in the ISO standard 10993-1 *Biological Evaluation of Medical Devices* including cytotoxicity, sensitization, skin irritation or intracutaneous reactivity, acute systemic toxicity, and hemocompatibility.

Testing was performed by an independent laboratory (NAMSA; Northwood, OH). Results of these tests, as listed in Tables 3a and 3b, support the biocompatibility of the Zenith TX2<sup>®</sup> TAA Endovascular Graft and the H&L-B One-Shot<sup>™</sup> Introduction System.

**Table 3a. Summary of Biocompatibility Testing – Zenith TX2® TAA Endovascular Graft**

Test Type	Purpose	Results	Pass/Fail
Cytotoxicity: ISO Elution Method (1X MEM Extract)	Determine whether extracts would cause cytotoxicity	Extract grade less than 2 on a scale of 0-4	Passed
Sensitization Study in the Guinea Pig (Maximization Method)	Evaluate the potential for delayed dermal contact sensitization	Test article extracts showed no evidence of causing delayed dermal contact sensitization in the guinea pig	Passed
Acute Intracutaneous Reactivity Study in the Rabbit (Extracts)	Determine whether extracts would cause local dermal irritant or toxic effects	Test scores were all $\leq 0.1$	Passed
Acute Systemic Toxicity Study in the Mouse (Extracts)	Determine whether extracts would cause acute systemic toxicity	No mortality or evidence of systemic toxicity from the extracts was observed	Passed
Subchronic Intravenous Toxicity Study in the Rat (14 day, Saline Extract)	Evaluate the potential for an extract to cause systemic toxicity following repeated intravenous injections	No significant evidence of systemic toxicity from the test extract	Passed
Genotoxicity: Bacterial Reverse Mutation Study (Extracts)	Evaluate whether extracts would cause mutagenic changes in <i>S. typhimurium</i> and <i>E. coli</i> strains	Spot plate inhibition screen – no inhibition observed; Standard plate incorporation assay – no 2 fold increase in mean number of revertants	Passed
Genotoxicity: <i>In Vitro</i> Chromosomal Aberration Study in Mammalian Cells (Extract)	Determine whether the extract would cause genotoxicity in Chinese Hamster ovary cells	Test extracts were concluded to be negative for the induction of structural chromosome aberrations: $\chi^2 = 0.0$ and $1.5$	Passed
Mouse Bone Marrow Micronucleus Study	Determine whether an extract would cause genotoxic changes in chromosomes or the mitotic apparatus of murine polychromatic erythrocytes	No statistically significant dose related increase in the number of micronucleated polychromatic erythrocytes was noted	Passed
Muscle Implantation Study in the Rabbit with Histopathology (Surgical Method, 4, 12, and 26 weeks)	Evaluate the potential for a local irritant or toxic response to material implanted in direct contact with muscle tissue	Macroscopic score – non-irritant Microscopic score – slight to moderate irritant	Acceptable
<i>In Vitro</i> Hemolysis Study (Modified ASTM – Extraction Method)	Determine whether extracts would cause hemolysis <i>in vitro</i>	0.0% hemolysis at 4 hrs	Passed
Plasma Recalcification Time Coagulation Study	Determine the potential of the test article to cause an effect on the coagulation cascade	Mild decrease in recalcification time	Passed
C3a Complement Activation Assay	Evaluate the potential to activate the complement system	Complement activation was comparable to the biomaterial control	Passed
Rabbit Pyrogen Study (Material Mediated)	Determine whether an extract induced a pyrogenic response following intravenous injection in rabbits	No temperature increase of 0.5 °C for any animal	Passed

**Table 3b. Summary of Biocompatibility Testing – H&L-B One-Shot™ Introduction System**

Test Type	Purpose	Results	Pass/Fail
Cytotoxicity Study Using the ISO Elution Method (1X MEM Extract) <sup>1</sup>	Determine whether extracts would cause cytotoxicity	Extract grade less than grade 2 on a scale of 0-4	Passed
Sensitization Study in the Guinea Pig (Maximization Method)	Evaluate the potential for delayed dermal contact sensitization	Test article extracts showed no evidence of causing delayed dermal contact sensitization	Passed
Acute Intracutaneous Reactivity Study in the Rabbit (Extracts)	Determine whether extracts would cause local dermal irritant or toxic effects following injections into skin	Test scores were all $\leq 0.5$	Passed
Acute Systemic Toxicity Study in the Mouse (Extracts)	Determine whether extracts would cause acute systemic toxicity following injection	No mortality or evidence of systemic toxicity from the extracts was observed	Passed
<i>In Vitro</i> Hemolysis Study (Modified ASTM – Extraction Method)	Determine whether the test article would cause hemolysis <i>in vitro</i>	Hemolytic index $\leq 2\%$ for all samples	Passed

**B. Product Testing**

A comprehensive laboratory (*in vitro*) testing plan for the Zenith TX2® TAA Endovascular Graft and H&L-B One-Shot™ Introduction System was developed to provide an assessment of device deployability, clinical/mechanical function, and integrity. The specific *in vitro* tests that were considered in assessing the Zenith TX2® TAA Endovascular Graft and H&L-B One-Shot™ Introduction System included tests listed in the testing standard *ISO 25539-1, Cardiovascular implants — Endovascular devices — Part 1: Endovascular prostheses*. The testing detailed in Table 4 verified the Zenith TX2® TAA Endovascular Graft and H&L-B One-Shot™ Introduction System met the product performance and design specifications. Results obtained from the *in vitro* testing provided evidence supporting the safety and effectiveness of the Zenith TX2® TAA Endovascular Graft and H&L-B One-Shot™ Introduction System.

**Table 4. Summary of Product Testing of the Zenith TX2® TAA Endovascular Graft and H&L-B One-Shot™ Introduction System**

Test	Samples Tested	Specification / Acceptance Criteria	Summary of Test Results
Profile/ Diameter Test	(24) 20 Fr systems (24) 22 Fr systems	Characterization study	Testing demonstrated the largest outer diameters for 20 Fr and 22 Fr systems were 7.70 mm and 8.68 mm, respectively.
Assessment of Hemostasis	(30) Check-Flo® Valves (30) Captor™ Valves	Significantly less leakage with Captor™ valve compared to established Check-Flo® valve	The established acceptance criterion was met.
Simulated Use Models	(24) Proximal components (24) Distal components	100% successful operation of each parameter pre-specified as important to proper deployment.	The established acceptance criteria were met.

Test	Samples Tested	Specification / Acceptance Criteria	Summary of Test Results
Visibility	(24) Proximal components (24) Distal components	100% successful visualization of each parameter pre-specified as important to proper deployment.	The established acceptance criteria were met.
Force to Deploy	(9) 22 Fr systems	Sheath Withdrawal < 100 N  Trigger Knob Removal < 36 N	The established acceptance criteria were met.
Bond Strength	At least 12 samples for each subassembly/bond type	Specified for each subassembly/bond type (minimum bond strength acceptance criteria ranged from >23N to >100N)	The established acceptance criteria were met.
Torsional Bond Strength	At least 9 samples for each subassembly/bond type	Minimum bond strength >0.068 N·m	The established acceptance criterion was met.
Bending Test	(30) Cannula subassemblies/bonds	Bond must not fail after cannula is bent 90°	The established acceptance criterion was met.
Bottom Cap Microscopic Inspection	(12) 22 Fr systems	Free from damage (e.g., pitting/gouging)	The established acceptance criterion was met.
Dimensional Verification	(12) Proximal components (12) Distal components (24) Tapered components (12) Proximal extensions (12) Distal extensions	Mean component length +/- 5% of stated length on package label  Mean component diameter +/- 5% of diameter stated on package label	The established acceptance criteria were met.
Water Permeability	(9) Graft material samples with sutures (24) Graft material samples without sutures	Mean permeability ≤350 ml/cm <sup>2</sup> /min	The established acceptance criterion was met.
Graft Material Mechanical Property Testing	Varies depending upon property	Characterization study	Mean longitudinal tensile strength ranged from 53.8 N/mm to 55.8 N/mm  Mean circumferential tensile strength ranged from 11.51 N/mm to 16.30 N/mm  Mean suture retention strength ranged from 13.6 N to 14.1 N
Flex/kink	(36) Proximal components (24) Tapered components (36) Proximal component / distal component pairs (24) Proximal component / proximal extension pairs (24) Distal component / distal extension pairs	Mean kink radius <35 mm	The established acceptance criterion was met.

Test	Samples Tested	Specification / Acceptance Criteria	Summary of Test Results
Migration Resistance	12 each of the barbed z-stent configurations	Mean pull-out force >8.14 N	The established acceptance criterion was met.
Pull Test for Modular Components	Multiple overlap conditions for each pair: (36) Proximal component / distal component pairs (24) Tapered component / distal component pairs (24) Proximal component / proximal extension pairs (24) Distal component / distal extension pairs	Characterization study	Mean separation forces for the conditions and combinations tested ranged from 2.4 N to 37 N.
Radial Force	3 of each z-stent configuration	Varies depending upon z-stent location with respect to graft material (acceptance criteria ranged from $\geq 0.8$ N to $\leq 13.4$ N)	The established acceptance criteria were met.
Graft-to-stent Attachment	(9) monofilament (9) braided – (intermediate knot) (9) braided – (start of knot)	>0.68 N for monofilament >6.7 N for braided	The established acceptance criteria were met.
Corrosion	(9) barb attachments at each of the following time-equivalent periods: 1, 3, 6, and 12 years (3) cannula attachments at each of the following time-equivalent periods: 1, 6, and 12 years; and (2) cannula attachments at the 3 year time-equivalent period	>0.68 N for barb attachment >0.68 N for cannula attachment	The established acceptance criteria were met.
Fatigue and Durability (pulsatile)	(8) Proximal component / distal component pairs	95% confidence that 95% of stents will not fracture after 10 years of cyclic (pulsatile) radial loading	The established acceptance criterion was met.
Fatigue and Durability (longitudinal)	(3) covered stents with barbs (3) uncovered stents with barbs	Failure of $\leq 4$ consecutive barbs at 400 million cycles (10 year time-equivalent)	The established acceptance criterion was met.
Stress/strain Analysis (FEA)	Computer analysis of each z-stent	Fatigue factor of safety >1.0	The established acceptance criterion was met.
Tensile Strength	(10) 0.020" stent wire samples (10) 0.011" barb wire samples N/A for 0.014", 0.016", and 0.018" wires – properties reported by vendor	Characterization study	Mean ultimate tensile strength ranged from 331 to 353 ksi.
MRI	(1) Proximal component / distal component pair	Demonstrates no known hazards to patients when subjected to 1.5T and 3.0T magnetic fields	The established acceptance criterion was met, supporting the device is MR Conditional

### C. Animal Studies

Table 5 summarizes the results of the definitive animal study.

**Table 5. Summary of definitive non-clinical *in vivo* study**

<b>Animal Study</b>	<b>Number &amp; Type of Animal</b>	<b>Test Article</b>	<b>Methods</b>	<b>Results/Conclusions</b>
Sub-chronic and chronic study of tubular endoprostheses	12 bovine animals	Zenith <sup>®</sup> components and the H&L-B <sup>™</sup> Introduction System sized for the animal anatomy	Catheter delivery and functionality were assessed sub-chronically and chronically in 12 animals. Three animals were maintained for 30 days, three were maintained for 90 days and six were maintained for 180 days.	All acceptance criteria were met. 100% successful deployment of the TX2 <sup>®</sup> in the intended position was achieved. 100% of the delivery systems and implants were able to be visualized. Patency was maintained in all devices until their explant at either 30, 90, or 180 days as evidenced by angiography and morphometric analysis. There was a 0% rate of migration in the animal study. Qualitative histopathological evaluation performed by an independent board-certified pathologist demonstrated minimal injury and inflammation

The Zenith TX2<sup>®</sup> TAA Endovascular Graft was evaluated in a focused animal study that evaluated the deployment procedure, the ability to visualize the delivery system and the implant in an *in vivo* setting, the migration resistance of the graft, the patency of the vessel and graft after implantation, animal survival, and histological evaluation of the biological response. This study demonstrates that the delivery system is capable of accessing the arterial vasculature, accurately deploying the Zenith TX2<sup>®</sup> TAA Endovascular Graft in its intended position, and effectively withdrawing it. The implant was shown to be capable of self-expanding into its deployed position and remaining patent and in position after implantation and throughout follow-up, demonstrating the effectiveness of the design. With the exception of one transient episode of mild fever, there were no adverse events in this study. Histological and pathological analyses demonstrated implantation of the Zenith TX2<sup>®</sup> TAA Endovascular Graft to be minimally traumatic and non-reactive in this study.

### D. Packaging, Shelf Life, and Sterilization Testing

Sterilization is accomplished with a validated sterilization process using Ethylene Oxide. This process has demonstrated a sterility assurance level of 10<sup>-6</sup>. Product and package stability testing of the Zenith TX2<sup>®</sup> TAA Endovascular Graft was performed and validated for a 3-year shelf life.

## X. SUMMARY OF CLINICAL STUDIES

### A. Study Design

The STARZ-TX2 Clinical Trial is a non-randomized, controlled, multi-center, study that was conducted to evaluate safety and effectiveness of the Zenith TX2<sup>®</sup> TAA Endovascular Graft in the elective treatment of patients with descending thoracic aortic aneurysms or ulcers, as compared to open surgical repair. The study consisted of an endovascular treatment group and an open surgical control group. The open surgical control group was comprised of both prospectively enrolled and retrospectively enrolled patients. The same inclusion/exclusion criteria applied to both the endovascular treatment group and open surgical control group, except that patients in the open surgical control group were not required to have anatomy amenable to endovascular repair with the Zenith TX2<sup>®</sup> TAA Endovascular Graft.

The study was designed to assess two primary and two secondary hypotheses regarding the endovascular treatment group compared to the open surgical control group. The primary hypothesis for safety was non-inferior 30-day survival, and the primary hypothesis for effectiveness was non-inferior 30-day rupture-free survival (i.e., freedom from rupture). The secondary hypotheses were superior clinical utility in the endovascular treatment group and non-inferior 30-day morbidity, expressed as a composite morbidity score including 57 pre-specified events. In addition, the study assessed survival, morbidity, and device performance through 12 months, and will continue these assessments at yearly intervals through 5 years.

In addition to covariate analysis, propensity score analysis was used to assess comparability of the groups. The control group was analyzed to justify the use of both retrospectively and prospectively enrolled patients.

FDA requested additional analyses, including the analysis of a composite effectiveness endpoint (freedom from a device event) and separate analyses of patients with aneurysms and patients with ulcers. The separate analyses for aneurysm patients and ulcer patients did not show any findings unique to the specific indications. Data for aneurysm and ulcer patients are presented separately where appropriate.

Patient imaging underwent independent core laboratory analysis. Adverse events, including all patient deaths, were adjudicated by an independent clinical events committee. A data safety monitoring board, comprised of independent physicians and a biostatistician, monitored the safety of the study.

### B. Patient Enrollment and Availability for Follow-up

Forty-two (42) institutions enrolled a total of 160 endovascular treatment patients and 70 (19 prospective and 51 retrospective) open surgical control patients, including 20 institutions that enrolled both endovascular treatment and open surgical control patients, 16 institutions that enrolled only endovascular treatment patients, and 6 institutions that enrolled only open surgical control patients. Although nearly 75% of the open surgical control patients were enrolled retrospectively, the endovascular treatment group and open surgical control groups proved to be largely contemporaneous; the earliest open surgical control patient was treated less than one year prior to investigational device exemption application (IDE) initiation, and 81% of the open surgical control patients were treated on or after the date on which the first endovascular patient was treated.

The study follow-up schedule for patients enrolled in the endovascular treatment group consisted of radiographic (CT scan and X-ray) and clinical assessments at pre-discharge, 30 days, 6 months, 12 months, and yearly thereafter through 5 years. The study follow-up schedule for patients enrolled in the open surgical control group consisted of radiographic (CT scan) and clinical assessments at pre-discharge (or 30 days) and 12 months, with an interim telephone contact at 6 months. Patient availability for study follow-up through 12 months as of September 12, 2007 is summarized in Table 6. Available data from on-going 24-month follow-up are also provided.

**Table 6. Follow-up Availability**

Timepoint	Eligible for follow-up (n)	Subjects with submitted data			Adequate imaging to assess parameter per core lab				Events occurring before next visit			
		Clinical	CT	X-ray	Size increase	Endoleak	Migration	Fracture	Death	Conversion	LTF	Not due for next visit
		% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	(n)	(n)	(n)
<b>Endovascular</b>												
Pre-discharge	158 <sup>a</sup>	100% (158)	94% (149)	98% (154)	n/a	85% (135)	n/a	96% (152)	3	0	0	0
30-day	155	94% (146)	92% (142)	87% (134)	78% (121)	81% (126)	72% (111)	88% (136)	5	0	5	0
6-month	145	90% (130)	89% (129)	85% (123)	81% (117)	79% (114)	77% (112)	88% (127)	5	0	5	0
12-month	135	94% (127)	92% (124)	85% (115)	83% (112)	76% (103)	79% (107)	91% (123)	10	0	4	25
24-month	96	70% (67)	61% (59)	63% (60)	58% (56)	59% (57)	57% (55)	66% (63)	n/a	n/a	n/a	n/a
<b>Open Surgical</b>												
Pre-discharge / 30-day	70	100% (70)	n/a	n/a	n/a	n/a	n/a	n/a	8	n/a	0	0
6-month	62	60% (37)	n/a	n/a	n/a	n/a	n/a	n/a	2	n/a	0	0
12-month	60	65% (39)	n/a	n/a	n/a	n/a	n/a	n/a	0	n/a	1	29 <sup>b</sup>
24-month	30	27% (8)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

n/a – not applicable

<sup>a</sup> Device insertion was not achieved in two patients.

<sup>b</sup> IRB/EC-approved follow-up was limited to 12 months at 11 sites that enrolled open surgical control patients (n=24); 5 patients not due for next visit.

### C. Demographic and Baseline Medical History Data

Table 7 compares the demographics and patient characteristics between the endovascular treatment group and open surgical control group.

**Table 7. Demographics and Patient Characteristics**

Demographic/characteristic	Endovascular	Open Surgical	Diff (95% CI) <sup>1</sup>	p value <sup>2</sup>
Age (years)	72.4 ± 9.6 (160)	67.6 ± 11.6 (70)	4.8 (1.9, 7.7)	<0.01
Gender				0.09
Male	72% (115/160)	60% (42/70)	12 (-1.6, 25)	
Female	28% (45/160)	40% (28/70)	-12 (-25, 1.6)	
Ethnicity <sup>3</sup>				0.82
Asian	2.5% (4/159)	1.4% (1/70)	1.1 (-2.6, 4.8)	
Black/African American	12% (19/159)	8.6% (6/70)	3.4 (-4.9, 12)	
Hispanic/Latino	3.8% (6/159)	4.3% (3/70)	-0.5 (-6.1, 5.1)	
White/Caucasian	80% (127/159)	86% (60/70)	-5.8 (-16, 4.5)	
Other	1.9% (3/159)	0.0% (0/70)	1.9 (n/a)	
Height (in)	67.5 ± 4.0 (154)	66.9 ± 3.6 (69)	0.6 (-0.5, 1.8)	0.26
Weight (lbs)	177 ± 35 (158)	167 ± 32 (70)	11 (1.1, 20)	0.02
Body mass index	27.2 ± 4.9 (153)	25.9 ± 3.7 (69)	1.3 (0.1, 2.5)	0.03

n/a – not applicable

<sup>1</sup> Confidence intervals are unadjusted for multiplicity and are based on the difference in means for continuous variables utilizing the T-distribution and the difference in percentages for categorical variables utilizing the Z-distribution.

<sup>2</sup> p values are based on Fisher's exact test for categorical variables and t-test for continuous variables and are unadjusted for multiplicity.

<sup>3</sup> Ethnicity reported as unknown in one patient.

Table 8 compares the medical history between the endovascular treatment group and open surgical control group.

**Table 8. Medical History**

Medical history	Endovascular	Open Surgical	Diff (95% CI) <sup>1</sup>	p value <sup>2</sup>
Cardiovascular				
Myocardial infarction	22.2% (35/158)	25% (17/68)	-2.9 (-15, 9.3)	0.73
Congestive heart failure	12.5% (20/160)	11.6% (8/69)	0.9 (-8.2, 10)	>0.99
Coronary artery disease	43.7% (69/158)	42% (29/69)	1.6 (-12, 16)	0.88
Arrhythmia	30.2% (48/159)	18.8% (13/69)	11 (-0.3, 23)	0.10
Vascular				
Thromboembolic event	10.1% (16/159)	8.7% (6/69)	1.4 (-6.8, 9.5)	>0.99
Peripheral vascular disease	24.4% (39/160)	26.1% (18/69)	-1.7 (-14, 11)	0.86
Family history of aneurysm	17.1% (24/140)	20.4% (11/54)	-3.2 (-16, 9.2)	0.67
Hypertension	89.4% (143/160)	82.9% (58/70)	6.5 (-3.5, 17)	0.19
Thoracic surgery/trauma	10% (16/160)	25.7% (18/70)	-16 (-27, -4.5)	<0.01
Diagnosed AAA	31.3% (50/160)	22.9% (16/70)	8.4 (-3.8, 21)	0.20
Repaired AAA	19.4% (31/160)	14.3% (10/70)	5.1 (-5.1, 15)	0.47
Chronic obstructive pulmonary disease	44.7% (71/159)	42.9% (30/70)	1.8 (-12, 16)	0.88
Renal failure requiring dialysis	3.1% (5/160)	2.9% (2/70)	0.3 (-4.5, 5.0)	>0.99
Diabetes	18.8% (30/160)	14.3% (10/70)	4.5 (-5.7, 15)	0.45

Medical history	Endovascular	Open Surgical	Diff (95% CI) <sup>1</sup>	p value <sup>2</sup>
Sepsis	1.9% (3/156)	1.5% (1/68)	0.5 (-3.1, 4.0)	>0.99
Neurologic				
Cerebrovascular accident	15.0% (24/160)	14.7% (10/68)	0.3 (-9.8, 10)	>0.99
Carotid endarterectomy	5.7% (9/159)	2.9% (2/70)	2.8 (-2.5, 8.1)	0.51
Gastrointestinal disease	40.5% (64/158)	30% (21/70)	11 (-2.7, 24)	0.14
Liver disease	6.3% (10/160)	4.3% (3/70)	2.0 (-4.1, 8.0)	0.75
Cancer	25.2% (40/159)	15.7% (11/70)	9.4 (-1.4, 20)	0.12
Excessive alcohol use	3.2% (5/157)	0.0% (0/67)	3.2 (n/a)	0.32
Tobacco use				0.19
Current smoker	22.4% (35/156)	17.6% (12/68)	4.8 (-6.4, 16)	
Quit smoking	66% (103/156)	61.8% (42/68)	4.3 (-9.5, 18)	
Never smoked	11.5% (18/156)	20.6% (14/68)	-9.1 (-20, 1.8)	
Access site				
Previous surgery	10.1% (16/159)	1.4% (1/69)	8.6 (3.2, 14)	0.02
Previous radiation	0.0% (0/159)	0.0% (0/69)	0 (n/a)	n/a
Allergies	43.8% (70/160)	40% (28/70)	3.8 (-10, 18)	0.66

n/a – not applicable

<sup>1</sup> Confidence intervals are unadjusted for multiplicity and are based on the difference in means for continuous variables utilizing the T-distribution and the difference in percentages for categorical variables utilizing the Z-distribution.

<sup>2</sup> p values are based on Fisher's exact test for categorical variables and t-test for continuous variables and are unadjusted for multiplicity.

Table 9 compares the results from patient risk assessment between the endovascular treatment group and open surgical control group.

**Table 9. Patient Risk Assessment**

Item <sup>1</sup>	Endovascular	Open Surgical	Diff (95% CI) <sup>2</sup>	p value <sup>3</sup>
ASA classification				< 0.01
Healthy patient (1)	8.8% (14/160)	7.1% (5/70)	1.6 (-5.9, 9.1)	
Mild systemic disease (2)	50% (80/160)	41.4% (29/70)	8.6 (-5.3, 22)	
Severe systemic disease (3)	36.9% (59/160)	28.6% (20/70)	8.3 (-4.7, 21)	
Incapacitating systemic disease (4)	4.4% (7/160)	22.9% (16/70)	-18 (-29, -8.2)	
Moribund patient (5)	0% (0/160)	0% (0/70)	0 (n/a)	
Total SVS-ISCVS risk score	6.4 ± 3.0 (159)	5.4 ± 3.5 (68)	1.0 (0.1, 1.9)	0.03

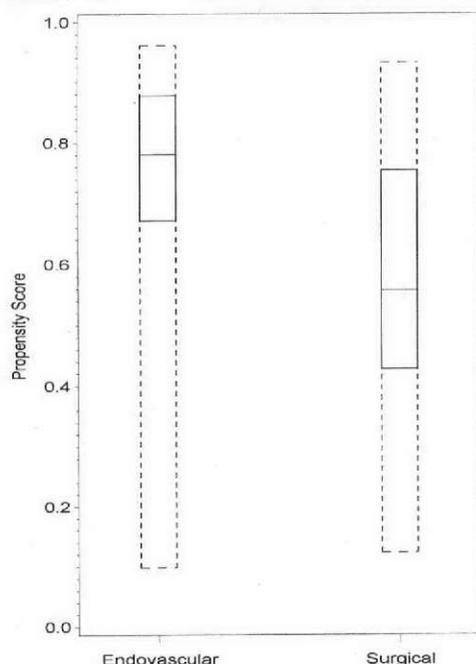
n/a – not applicable

<sup>1</sup> The SVS-ISCVS scoring system may be considered more objective than the ASA classification; however, direct comparisons of key patient characteristics are provided in Tables 7 and 8.

<sup>2</sup> Confidence intervals are unadjusted for multiplicity and are based on the difference in means for continuous variables utilizing the T-distribution and the difference in percentages for categorical variables utilizing the Z-distribution.

<sup>3</sup> p values are based on Fisher's exact test for categorical variables and t-test for continuous variables and are unadjusted for multiplicity.

Covariate and propensity score analyses supported the appropriateness of comparisons between study groups. A representative plot of propensity score quartiles is presented in Figure 11.



**Figure 11. Quartiles of the Propensity Scores for the Two Study Groups**

#### **D. Baseline Anatomical Data**

Table 10 compares the morphology type, location, and size between the endovascular treatment group and open surgical control group based on the results from core lab analysis.

**Table 10. Morphology Type, Location and Size**

Item	Endovascular	Open Surgical	Diff (95% CI) <sup>1</sup>	p value <sup>2</sup>
Morphology type				0.40
Aneurysm	85.6% (137/160)	90.0% (63/70) <sup>4</sup>	-4.4 (-13, 4.5)	
Ulcer <sup>3</sup>	14.4% (23/160)	10.0% (7/70)	4.4 (-4.5, 13)	
Morphology location <sup>5</sup>				0.02
Proximal	22.5% (36/160)	36.9% (24/65)	-14 (-28, -1.0)	
Middle	55.0% (88/160)	52.3% (34/65)	2.7 (-12, 17)	
Distal	22.5% (36/160)	10.8% (7/65)	12 (1.8, 22)	
Aneurysm size				
Major axis diameter (mm)	60.8 ± 10.7 (137)	63.0 ± 10.8 (53)	-2.2 (-5.6, 1.2)	0.20
Minor axis diameter (mm)	50.8 ± 10.5 (137)	57.5 ± 9.3 (49)	-6.7 (-10, -3.3)	<0.01
Length (mm)	151 ± 71.3 (132)	158.6 ± 81.0 (46)	-7.9 (-33, 17)	0.53
Ulcer size				
Major axis diameter (mm)	28.7 ± 9.7 (22)	29.0 ± 7.3 (7)	-0.2 (-8.4, 8.0)	0.95
Minor axis diameter (mm)	20.9 ± 7.7 (23)	21.1 ± 9.8 (7)	-0.1 (-7.4, 7.1)	0.96
Depth (mm)	14.4 ± 4.7 (22)	20.7 ± 7.8 (7)	-6.3 (-11, -1.4)	0.01

n/a – not applicable

<sup>1</sup> Confidence intervals are unadjusted for multiplicity and are based on the difference in means for continuous variables utilizing the T-distribution and the difference in percentages for categorical variables utilizing the Z-distribution.

<sup>2</sup> p values are based on Fisher's exact test for categorical variables and t-test for continuous variables and are unadjusted for multiplicity.

<sup>3</sup> Ulcers ≥10 mm in depth and 20 mm in diameter were eligible for study inclusion.

<sup>4</sup>As determined by site assessment for 7 open surgical patients without available imaging for core lab analysis.

<sup>5</sup> Primary location described as proximal one-third (i.e., arch to T6), middle one-third (i.e., T6-T8), or distal one-third (i.e., T9-L2).

### E. Devices Implanted

Endovascular patients were treated using either a two-piece main body (proximal main body component in combination with a distal main body component) or a one-piece main body (either a proximal main body component only or a one-piece main body component). Table 11 reports the percent of endovascular patients treated with a two-piece main body and the percent of patients treated with a one-piece main body. Also reported is the total number of components deployed during the initial implant procedure for patients treated with a two-piece main body and for patients treated with a one-piece main body in order to account for ancillary component use.

**Table 11. Main Body System Type and Total Number of Components**

Type	% (n)	Total number of components (main body and ancillary)			
		1	2	3	4
Two-piece	59.5% (94/158)	n/a	88.3% (83/94)	11.7% (11/94)	0% (0/94)
One-piece	40.5% (64/158)	90.6% (58/64) <sup>1</sup>	7.8% (5/64)	1.6% (1/64)	0% (0/64)

<sup>1</sup>One patient received a proximal extension as the principal endograft.

Table 12 reports the number of components (main body components and main body extensions) used during the initial implant procedure, by diameter.

**Table 12. Graft Diameters Implanted during Initial Procedure**

Diameter (mm)	Non-tapered proximal main body component <sup>1</sup> (n)	Tapered proximal main body component <sup>1</sup> (n)	Distal main body component <sup>1</sup> (n)	One-piece main body component (n)	Proximal extension (n)	Distal extension (n)
28	4	n/a	2	0	0	1
30	8	n/a	2	2	1	0
32	13	2	7	0	1	1
34	22	1	14	1	2	2
36	19	3	17	0	3	1
38	22	7	22	0	0	0
40	29	5	20	0	0	4
42	12	7	10	0	2	1

<sup>1</sup>Multiple length increments available for each diameter.

## F. Safety Results

### Survival

The primary safety hypothesis was based on 30-day survival, which was non-inferior ( $p < 0.01$ ) in the endovascular treatment group compared to the open surgical control group (98.1% vs. 94.3%). As illustrated by Figure 12 and presented in Table 13, 365-day survival from all-cause mortality was 91.6% in the endovascular treatment group and 85.5% in the open surgical control group. Survival from all-cause mortality at 730 days is 79.8% in the endovascular treatment group and 85.5% in the open surgical control group, with follow-up on-going.

Survival from aneurysm-related mortality (i.e., death occurring within 30 days of the initial implant procedure or a secondary intervention, or any death adjudicated to be aneurysm-related by the independent clinical events committee) through 365 days was 94.2% in the endovascular treatment group and 88.2% in the open surgical control group, as illustrated by Figure 13 and presented in Table 14. Survival from aneurysm-related mortality at 730 days is 92.9% in the endovascular treatment group and 88.2% in the open surgical control group, with follow-up on-going.

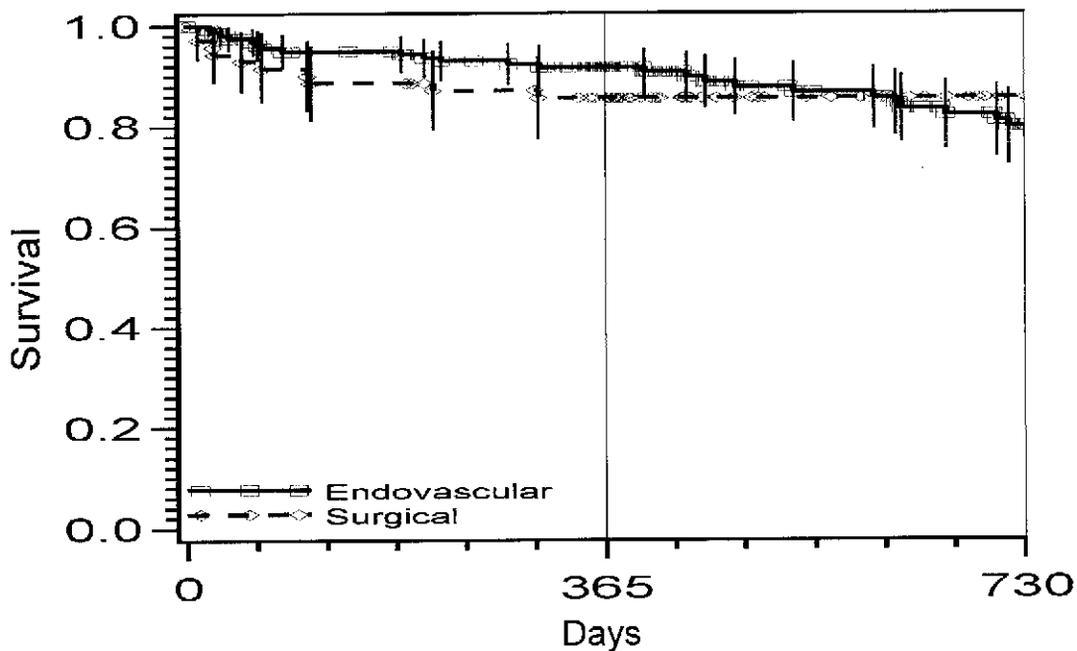
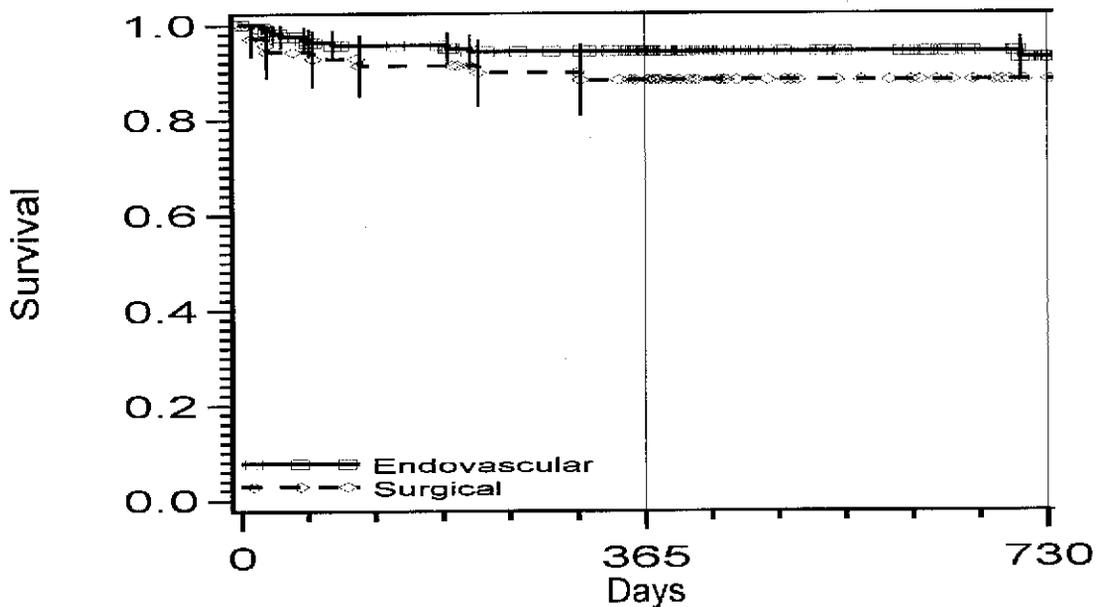


Figure 12. Survival from All-Cause Mortality through 730 Days

**Table 13. Kaplan-Meier All-cause Mortality Survival Estimates**

Arm	Days	Kaplan-Meier Estimate	Standard Error	Cumulative Events	Cumulative Censored	Patients Remaining
Endovascular	0	1.000	0.0000	0	0	160
	30	0.981	0.0107	3	1	156
	365	0.916	0.0223	13	28	119
	730	0.798	0.0387	24	78	58
Open Surgical	0	1.000	0.0000	0	0	70
	30	0.943	0.0277	4	0	66
	365	0.855	0.0423	10	7	53
	730	0.855	0.0423	10	45	15



**Figure 13. Survival from Aneurysm-Related Mortality through 730 Days**

**Table 14. Kaplan-Meier TAA-related Mortality Survival Estimates**

Arm	Days	Kaplan-Meier Estimate	Standard Error	Cumulative Events	Cumulative Censored	Patients Remaining
Endovascular	0	1.000	0.0000	0	0	160
	30	0.981	0.0107	3	1	156
	365	0.942	0.0187	9	32	119
	730	0.929	0.0229	10	92	58
Open Surgical	0	1.000	0.0000	0	0	70
	30	0.943	0.0277	4	0	66
	365	0.882	0.0391	8	9	53
	730	0.882	0.0391	8	47	15

## Morbidity

A secondary hypothesis was based on 30-day morbidity with endovascular treatment, expressed as a composite morbidity score (mean number of events per patient), which, as shown in Table 15, was non-inferior in the endovascular treatment group compared to the open surgical control group ( $p < 0.01$ ).

**Table 15. Total Morbidity Score within 0-30 Days**

Item	Endovascular	Open Surgical	Diff (95% CI) <sup>1</sup>	p value <sup>2</sup>
30-day morbidity score (events <sup>3</sup> per patient)	1.3 ± 3.0 (160)	2.9 ± 3.6 (70)	-1.6 (-2.5, -0.7)	<0.01

<sup>1</sup> Confidence interval on the difference in means utilized the T-distribution and is unadjusted for multiplicity.

<sup>2</sup> p value is based on test for non-inferiority and is unadjusted for multiplicity.

<sup>3</sup> Pre-specified events that were considered for the morbidity score included: cardiovascular events (Q-wave myocardial infarction; non-Q-wave myocardial infarction; congestive heart failure; arrhythmia requiring intervention or new treatment; cardiac ischemia requiring intervention; inotropic support; refractory hypertension [systolic BP of >160 despite receiving medication]; cardiac event involving arrest, resuscitation, or balloon pump); pulmonary events (ventilation >24 hours; re-intubation; pneumonia requiring antibiotics; supplemental oxygen at time of discharge; chronic obstructive pulmonary disease; pleural effusion requiring treatment; pulmonary edema requiring treatment; pneumothorax; hemothorax; pulmonary event requiring tracheostomy or chest tube); renal events (urinary tract infection requiring antibiotic treatment; renal failure requiring dialysis; renal insufficiency [serum creatinine rise >30% from baseline resulting in a persistent value >2.0 mg/dL]; permanent dialysis, hemofiltration, or kidney transplant in patient with normal pre-procedure creatinine); gastrointestinal events (bowel/mesenteric ischemia; gastrointestinal infection requiring treatment; gastrointestinal bleeding requiring treatment; paralytic ileus >4 days; bowel resection); neurological events (stroke; TIA/RIND; carotid artery embolization/occlusion; paraparesis/spinal cord shock; paraplegia); vascular events (pulmonary embolism; pulmonary embolism involving hemodynamic instability or surgery; vascular injury; aneurysm leak/rupture; aneurysm or vessel leak requiring re-operation; pseudoaneurysm requiring surgical repair; increase in aneurysm size >0.5 cm relative to first post-procedure measurement; aorto-esophageal fistula; aorto-bronchial fistula; aorto-enteric fistula; arterial thrombosis; embolization resulting in tissue loss or requiring intervention; amputation involving more than the toes; deep vein thrombosis; deep vein thrombosis requiring surgical or lytic therapy; hematoma requiring surgical repair; hematoma requiring receipt of blood products; coagulopathy requiring surgery; post-procedure transfusion); wound events (wound infection requiring antibiotic treatment; incisional hernia; lymph fistula; wound breakdown requiring debridement; seroma requiring treatment; wound complication requiring return to the operating room).

The 30-day and 365-day Kaplan-Meier estimates for freedom from any one of the following pre-specified events (representing a subset of the events listed in Table 15) are illustrated in Figure 14 and reported in Table 16, along with the estimates for each individual event: Q-wave MI; cardiac event involving arrest, resuscitation, or balloon pump; ventilation >72 hours; re-intubation; pulmonary event requiring a tracheostomy or chest tube; permanent dialysis, hemofiltration, or transplant [in a patient with normal pre-procedure creatinine]; bowel resection; stroke; paraplegia; pulmonary embolism involving hemodynamic instability or requiring surgery; aneurysm or vessel leak requiring re-operation; amputation involving more than the toes; deep vein thrombosis requiring surgery or lytic therapy; coagulopathy requiring surgery; and wound complication requiring return to OR.

The 30-day estimate for freedom from any of the events from this pre-specified subset was 90.6% in the endovascular treatment group and 67.1% in the open surgical control group. The 365-day estimate for freedom from these events was 87.3% in the endovascular treatment group and 64.3% in the open surgical control group. The 730 day estimate for freedom from any of the events from the pre-specified subset is 83.6% in the endovascular treatment group and 64.3% in the open surgical control group, with follow-up on-going.

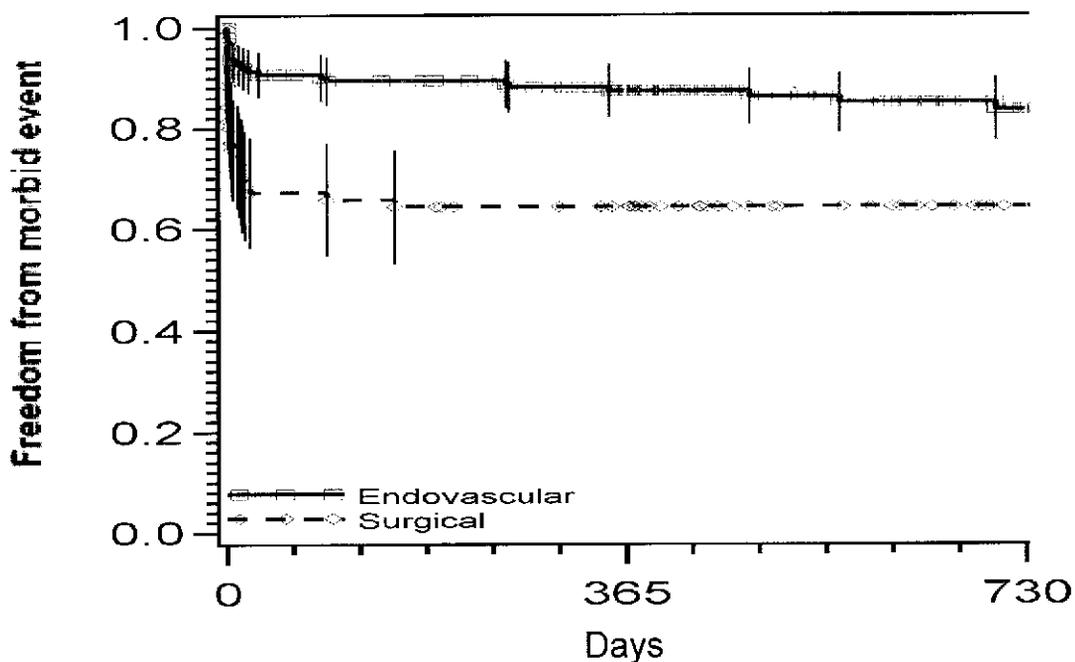


Figure 14. Freedom from Pre-specified Subset of Morbid Events through 730 Days

Table 16. Summary of Kaplan-Meier Estimates for Freedom from Pre-specified Subset of Morbid Events\*

Event	Parameter	30 days		365 days		730 days	
		Endo	Open	Endo	Open	Endo	Open
Any event	Number at risk <sup>1</sup>	160	70	144	47	109	39
	Cumulative events	15	23	20	25	23	25
	Cumulative censored <sup>2</sup>	1	0	31	6	84	35
	Kaplan-Meier est. <sup>3</sup>	0.91	0.67	0.87	0.64	0.84	0.64
	Standard error	0.02	0.06	0.03	0.06	0.3	0.06
Q-wave MI	Number at risk <sup>1</sup>	160	70	156	66	119	53
	Cumulative events	0	0	0	0	0	0
	Cumulative censored <sup>2</sup>	4	4	41	17	102	55
	Kaplan-Meier est. <sup>3</sup>	1.00	1.00	1.00	1.00	1.00	1.00
	Standard error	0.00	0.00	0.00	0.00	0.00	0.00
Cardiac event involving arrest, resuscitation or balloon pump	Number at risk <sup>1</sup>	160	70	153	66	118	53
	Cumulative events	4	1	4	2	5	2
	Cumulative censored <sup>2</sup>	3	3	38	15	98	53
	Kaplan-Meier est. <sup>3</sup>	0.98	0.99	0.98	0.97	0.96	0.97
	Standard error	0.01	0.01	0.01	0.02	0.02	0.02
Vent. >72 hours	Number at risk <sup>1</sup>	160	70	155	57	119	46
	Cumulative events	1	11	1	11	1	11
	Cumulative censored <sup>2</sup>	4	2	40	13	101	47
	Kaplan-Meier est. <sup>3</sup>	0.99	0.84	0.99	0.84	0.99	0.84

Event	Parameter	30 days		365 days		730 days	
		Endo	Open	Endo	Open	Endo	Open
	Kaplan-Meier est. <sup>3</sup> Standard error	0.01	0.04	0.01	0.04	0.01	0.04
Re-intubation	Number at risk <sup>1</sup>	160	70	150	57	117	47
	Cumulative events	8	10	8	11	9	11
	Cumulative censored <sup>2</sup>	2	3	35	12	94	47
	Kaplan-Meier est. <sup>3</sup> Standard error	0.95	0.86	0.95	0.84	0.94	0.84
Pulmonary event requiring tracheostomy or chest tube	Number at risk <sup>1</sup>	160	70	154	59	118	49
	Cumulative events	2	9	4	12	5	12
	Cumulative censored <sup>2</sup>	4	2	38	9	97	45
	Kaplan-Meier est. <sup>3</sup> Standard error	0.99	0.87	0.97	0.82	0.96	0.82
Permanent dialysis or transplant	Number at risk <sup>1</sup>	160	70	156	66	119	53
	Cumulative events	0	0	0	0	0	0
	Cumulative censored <sup>2</sup>	4	4	41	17	102	55
	Kaplan-Meier est. <sup>3</sup> Standard error	1.00	1.00	1.00	1.00	1.00	1.00
Bowel resection	Number at risk <sup>1</sup>	160	70	153	65	117	52
	Cumulative events	3	1	5	1	5	1
	Cumulative censored <sup>2</sup>	4	4	38	17	98	54
	Kaplan-Meier est. <sup>3</sup> Standard error	0.98	0.99	0.97	0.99	0.97	0.99
Stroke	Number at risk <sup>1</sup>	160	70	153	63	117	50
	Cumulative events	4	6	5	7	6	7
	Cumulative censored <sup>2</sup>	3	1	38	13	98	48
	Kaplan-Meier est. <sup>3</sup> Standard error	0.98	0.91	0.97	0.90	0.95	0.90
Paraplegia	Number at risk <sup>1</sup>	160	70	155	63	119	53
	Cumulative events	2	4	2	4	2	4
	Cumulative censored <sup>2</sup>	3	3	39	13	100	51
	Kaplan-Meier est. <sup>3</sup> Standard error	0.99	0.94	0.99	0.94	0.99	0.94
PE involving hemodynamic instability or surgery	Number at risk <sup>1</sup>	160	70	156	66	119	53
	Cumulative events	0	0	0	0	0	0
	Cumulative censored <sup>2</sup>	4	4	41	17	102	55
	Kaplan-Meier est. <sup>3</sup> Standard error	1.00	1.00	1.00	1.00	1.00	1.00
Aneurysm or vessel leak requiring re-operation	Number at risk <sup>1</sup>	160	70	156	65	119	52
	Cumulative events	0	1	0	1	0	1
	Cumulative censored <sup>2</sup>	4	4	41	17	102	54
	Kaplan-Meier est. <sup>3</sup> Standard error	1.00	0.99	1.00	0.99	1.00	0.99

Event	Parameter	30 days		365 days		730 days	
		Endo	Open	Endo	Open	Endo	Open
	Kaplan-Meier est. <sup>3</sup> Standard error	0.00	0.01	0.00	0.01	0.00	0.01
Amputation involving more than toes	Number at risk <sup>1</sup>	160	70	156	66	119	53
	Cumulative events	0	0	0	1	0	1
	Cumulative censored <sup>2</sup>	4	4	41	16	102	54
	Kaplan-Meier est. <sup>3</sup>	1.00	1.00	1.00	0.98	1.00	0.98
	Standard error	0.00	0.00	0.00	0.02	0.00	0.02
Deep vein thrombosis requiring surgery or lytic therapy	Number at risk <sup>1</sup>	160	70	156	66	119	53
	Cumulative events	0	0	1	0	1	0
	Cumulative censored <sup>2</sup>	4	4	40	17	101	55
	Kaplan-Meier est. <sup>3</sup>	1.00	1.00	0.99	1.00	0.99	1.00
	Standard error	0.00	0.00	0.01	0.00	0.01	0.00
Coagulopathy requiring surgery	Number at risk <sup>1</sup>	160	70	156	65	119	52
	Cumulative events	0	1	0	1	0	1
	Cumulative censored <sup>2</sup>	4	4	41	17	102	55
	Kaplan-Meier est. <sup>3</sup>	1.00	0.99	1.00	0.99	1.00	0.99
	Standard error	0.00	0.01	0.00	0.01	0.00	0.01
Wound complication requiring return to OR	Number at risk <sup>1</sup>	160	70	156	66	117	53
	Cumulative events	0	0	2	0	2	0
	Cumulative censored <sup>2</sup>	4	4	41	17	100	55
	Kaplan-Meier est. <sup>3</sup>	1.00	1.00	0.99	1.00	0.99	1.00
	Standard error	0.00	0.00	0.01	0.00	0.01	0.00

\*Subset of events pre-selected from list in Table 15 prior to start of the study by the physician steering committee.

<sup>1</sup> Number of patients at risk at the beginning of the interval

<sup>2</sup> Total censored patients up to and including the specific interval

<sup>3</sup> Made at end of interval

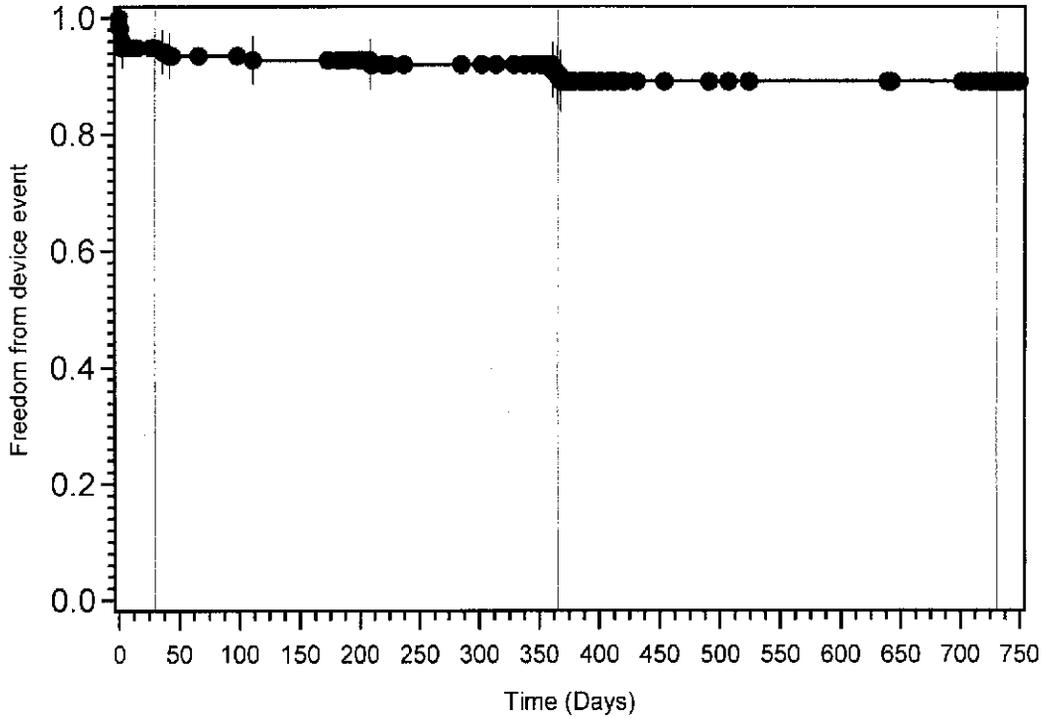
## G. Effectiveness Results

### Freedom from Rupture

The primary effectiveness hypothesis was based on 30-day rupture-free survival (i.e., freedom from rupture), which was non-inferior ( $p < 0.01$ ) in the endovascular treatment group compared to the open surgical control group (100% vs. 100%). Because there were no ruptures in either group, the planned analysis (Blackwelder) could not be performed, and an alternate analysis (exact non-inferiority test) was necessary to generate the  $p$  value. Freedom from rupture was 100% in both groups through 365 days post-procedure. Freedom from rupture is 100% in both groups through 730 days post-procedure, with follow-up on-going.

**Freedom from Device Events**

The results from Kaplan-Meier analysis for freedom from any of the following device events are illustrated in Figure 15 and presented in Table 17: technical failure; loss of patency; rupture; secondary intervention; conversion; stent fracture; Type I or III endoleak; or migration. Freedom from any device event was 94.9% at 30 days and 90.1% at 365 days. Freedom from any device event at 730 days is 89.1%, with follow-up on-going.



**Figure 15. Freedom from Device Events**

**Table 17. Kaplan-Meier Estimate for Freedom from Device Events**

Days	Kaplan-Meier Estimate	Standard Error	Lower 95% Confidence Limit	Upper 95% Confidence Limit	Cumulative Events	Cumulative Censored	Patients Remaining
30	0.949	0.0176	0.914	0.983	8	14	138
365	0.901	0.0254	0.851	0.951	14	55	91
730	0.891	0.0271	n/a	n/a	15	105	40

### Change in Size

Table 18 reports the percent of patients with an increase (>5 mm), decrease (>5 mm), or no change (≤5 mm) in aneurysm diameter or ulcer depth at each follow-up timepoint subsequent to pre-discharge (baseline) based on the results from core lab analysis. In total, 9 patients (7 aneurysm, 2 ulcer) experienced an increase in size within 12 months, with no new cases of growth identified at the 24-month follow-up, which remains on-going.

**Table 18. Percent of Endovascular Treatment Patients with an Increase, Decrease, or No Change in Aneurysm/Ulcer Size Based on Core Lab Analysis**

Timepoint	Combined % (n)	Aneurysm % (n)	Ulcer % (n)
30-day			
Increase (>5 mm)	0.8% (1/121) <sup>1</sup>	1.0% (1/105)	0% (0/16)
Decrease (>5 mm)	6.6% (8/121)	5.7% (6/105)	12.5% (2/16)
No change (≤5 mm)	92.6% (112/121)	93.3% (98/105)	87.5% (14/16)
6-month			
Increase (>5 mm)	3.4% (4/117) <sup>2</sup>	3.1% (3/98)	5.3% (1/19)
Decrease (>5 mm)	33.3% (39/117)	33.7% (33/98)	31.6% (6/19)
No change (≤5 mm)	63.2% (74/117)	63.3% (62/98)	63.2% (12/19)
12-month			
Increase (>5 mm)	7.1% (8/112) <sup>3</sup>	7.2% (7/97)	6.7% (1/15)
Decrease (>5 mm)	48.2% (54/112)	50.5% (49/97)	33.3% (5/15)
No change (≤5 mm)	44.6% (50/112)	42.3% (41/97)	60% (9/15)
24-month			
Increase (>5 mm)	1.8% (1/56) <sup>4</sup>	0% (0/49)	14.3% (1/7)
Decrease (>5 mm)	53.6% (30/56)	57.1% (28/49)	28.6% (2/7)
No change (≤5 mm)	44.6% (25/56)	42.9% (21/49)	57.1% (4/7)

<sup>1</sup> This aneurysm patient is also counted as an increase at 6 and 12 months, was without detectable endoleak or evidence of graft infection, and was found to have a decrease in size at the 24-month follow-up (without secondary intervention).

<sup>2</sup> Includes three new patients (2 aneurysm, 1 ulcer). Both aneurysm patients are also counted as an increase at 12 months. One aneurysm patient had no detectable endoleak or evidence of graft infection and was found to have no change in size at 24 months (without secondary intervention). The other aneurysm patient also had no detectable endoleak or evidence of graft infection, but had an aortic neck diameter at the location of actual graft placement that does not meet the recommended oversizing of at least 10% as well as an inverted funnel-shaped proximal neck and a funnel-shaped distal neck. This same patient also underwent two secondary interventions for aneurysm growth and expired within 30 days of the later secondary intervention (after removal of ventilator support following a stroke). The ulcer patient, who was noted to have a Type II endoleak at pre-discharge, was found to have no change in size at 12 months and 24 months (without secondary intervention).

<sup>3</sup> Includes five new patients (4 aneurysm, 1 ulcer). In three of the aneurysm patients, each of which are awaiting further follow-up, there was no detectable endoleak or evidence of graft infection, but the aortic neck diameter at the location of actual graft placement does not meet the recommended oversizing of at least 10%, and there was also an inverted funnel-shaped proximal aortic neck and a funnel-shaped distal aortic neck. The other new aneurysm patient was noted to have a distal Type I endoleak, underwent two secondary interventions, and is awaiting further follow-up. In the new ulcer patient, who also exhibited growth at 24 months, there was no detectable endoleak or evidence of graft infection, but the aortic neck diameter at the location of actual graft placement does not meet the recommended oversizing of at least 10%.

<sup>4</sup> This ulcer patient was first noted to have growth at 12 months, as discussed in note '3'.

## Endoleak

Table 19 reports the percent of patients with endoleak (by type) at each follow-up timepoint based on the results from core lab analysis.

**Table 19. Percent of Endovascular Treatment Patients with Endoleak (New and Persistent) Based on Core Lab Analysis**

Type	Timepoint				
	Pre-discharge	30-day	6-month	12-month	24-month
Any (new only)	12.6% (17/135)	1.6% (2/126) <sup>a,b</sup>	0% (0/114)	1.0% (1/103) <sup>c</sup>	0% (0/57)
Any (new and persistent)	12.6% (17/135)	4.8% (6/126)	2.6% (3/114)	3.9% (4/103)	1.8% (1/57)
Multiple	0% (0/135)	0% (0/126)	0% (0/114)	0% (0/103)	0% (0/57)
Proximal Type I	0% (0/135)	0% (0/126)	0% (0/114)	0% (0/103)	0% (0/57)
Distal Type I	0.7% (1/135)	0.8% (1/126)	0.9% (1/114)	0% (0/103)	0% (0/57)
Type IIa	1.5% (2/135)	0.8% (1/126) <sup>a</sup>	0% (0/114)	0% (0/103)	0% (0/57)
Type IIb	5.9% (8/135)	2.4% (3/126)	1.8% (2/114)	1.9% (2/103)	1.8% (1/57)
Type III	1.5% (2/135)	0.8% (1/126) <sup>b</sup>	0% (0/114)	1.0% (1/103) <sup>b</sup>	0% (0/57)
Type IV	1.5% (2/135)	0% (0/126)	0% (0/114)	0% (0/103)	0% (0/57)
Unknown	1.5% (2/135)	0% (0/126)	0% (0/114)	1.0% (1/103) <sup>c</sup>	0% (0/57)

<sup>a</sup>Type IIa in one patient who did not undergo endoleak assessment at pre-discharge.

<sup>b</sup>Non-junctional Type III endoleak in one patient that was not evident at pre-discharge or 6-months, is not associated with aneurysm growth, has not required reintervention, and is awaiting further follow-up.

<sup>c</sup>Unknown Type endoleak, but in a patient who previously had a Type IIb endoleak at pre-discharge and no endoleak at 30 days or 6 months.

## Migration

Table 20 reports the percent of patients with core lab-identified and CEC-confirmed migration (>10 mm) at each follow-up timepoint (date of first occurrence). There have been no patients with clinically significant migration (i.e., migration resulting in endoleak, growth, or requiring secondary intervention).

**Table 20. Percent of Patients with CEC-Confirmed Migration (Date of First Occurrence)**

Item	30-day	6-month	12-month	24-month
Migration (>10 mm)	0% (0/111)	0.9% (1/112)*	1.9% (2/106)*	1.8% (1/55)*

Includes two cases of caudal migration of the proximal graft and two cases of cranial migration of the distal graft. All patients have an aortic neck diameter at the location of actual graft placement that does not meet the recommended oversizing of at least 10%. Additionally, three also have placement of the pertinent barbed stent in a neck that is either an acutely angled segment or in an area of thrombus.

### Device Integrity

Table 21 reports the percent of patients with device integrity findings at each follow-up timepoint based on the results from core lab analysis. One patient was noted to have a device integrity finding: entanglement of neighboring struts of the distal bare stent, which has not been associated with migration, endoleak, or the need for secondary intervention.

**Table 21. Percent of Endovascular Treatment Patients with Device Integrity Findings by Core Lab**

Finding	Timepoint				
	Pre-discharge	30-day	6-month	12-month	24-month
Stent fracture	0% (0/152)	0% (0/136)	0% (0/127)	0% (0/123)	0% (0/63)
Barb separation	0% (0/152)	0% (0/136)	0% (0/127)	0% (0/123)	0% (0/63)
Stent-to-graft separation	0% (0/152)	0% (0/136)	0% (0/127)	0% (0/123)	0% (0/63)
Component separation	0% (0/152)	0% (0/136)	0% (0/127)	0% (0/123)	0% (0/63)
Other	0.7% (1/152) <sup>1</sup>	0% (0/136)	0% (0/127)	0.8% (1/123) <sup>1</sup>	0% (0/63)

<sup>1</sup>Entanglement of neighboring struts of distal bare stent; same patient at pre-discharge and 12 months; finding not associated with migration, endoleak, or the need for secondary intervention.

### Kink, Compression, and Patency

Table 22 reports the results from core lab assessment for endovascular graft kink (evidence of reduced graft diameter or narrowing of lumen in the presence of acute aortic angulation), compression (evidence of reduced graft diameter or narrowing of the lumen in the absence of aortic angulation), and loss of patency. Three patients were noted to have a kink at one or more timepoints and two patients were noted to have compression at one or more timepoints. None required a secondary intervention.

**Table 22. Endovascular Graft Kink, Compression, and Loss of Patency by Core Lab Analysis**

Finding	Timepoint				
	Pre-discharge	30-day	6-month	12-month	24-month
Kink	1.9% (3/155)	0.7% (1/139)	0.8% (1/127)	1.6% (2/123)	0% (0/63)
Compression	1.4% (2/142) <sup>a</sup>	0.8% (1/124) <sup>a</sup>	0.9% (1/117) <sup>a</sup>	0.9% (1/108) <sup>a</sup>	2.1% (1/47) <sup>a</sup>
Loss of patency	0% (0/138)	0% (0/126)	0% (0/114)	0% (0/103)	0% (0/57)

<sup>a</sup>Concentric constriction of one mid-body stent of the device not associated with tortuosity or flow limitation with expansion of the stents above and below the compressed segment -- this should be distinguished from the phenomena of endovascular graft collapse described in literature for other (non-Zenith) grafts.

### Re-interventions

Seven (4.4%) endovascular treatment patients (6 aneurysm, 1 ulcer) and four (5.7%) open surgical control patients (2 aneurysm, 2 ulcer) underwent at least one re-intervention within 365 days subsequent to the initial aneurysm/ulcer repair procedure. The reasons for re-intervention are reported in Table 23. There have been no conversions to open surgical repair in the endovascular treatment group.

**Table 23. Reasons for Secondary Intervention**

Reason	Endovascular			Open Surgical		
	0-30 days	31-365 days	366-730 days	0-30 days	31-365 days	366-730 days
Aneurysm rupture	0	0	0	0	0	0
Component separation	0	0	0	n/a	n/a	0
Symptoms	0	0	0	1 <sup>f</sup>	0	0
Occlusion	0	0	0	0	0	0
Device stenosis	0	0	0	n/a	n/a	n/a
Device kink	0	0	0	n/a	n/a	n/a
Device migration	0	0	0	n/a	n/a	n/a
Infection	0	0	0	0	0	0
Endoleak	3	2 <sup>a</sup>	0			
Proximal Type I	1 <sup>b</sup>	0	0			
Distal Type I	1 <sup>c</sup>	2 <sup>a</sup>	0			
Type IIa	0	0	0	n/a	n/a	n/a
Type IIb	0	0	0			
Type III	1 <sup>d</sup>	0	0			
Type IV	0	0	0			
Unknown	0	0	0			
Other	0	3 <sup>e</sup>	1 <sup>i</sup>	3 <sup>g</sup>	1 <sup>h</sup>	0

n/a – not applicable

<sup>a</sup> One aneurysm patient with two interventions for a distal Type I endoleak – bare stent placement and stent placement/coil embolization/distal extension placement.

<sup>b</sup> Aneurysm patient treated with proximal main body extension placement.

<sup>c</sup> Aneurysm patient treated with molding balloon angioplasty and distal extension placement

<sup>d</sup> Aneurysm patient underwent angiogram to rule out endoleak.

<sup>e</sup> Includes one ulcer patient with iliac artery occlusion, treated with femoral-femoral bypass; one aneurysm patient with growth, treated with distal extension placement in overlap and distal end of graft; and one aneurysm patient who developed a pseudoaneurysm at follow-up, treated with proximal extension placement.

<sup>f</sup> One ulcer patient with multiple reasons of symptoms and other (continued bleeding), treated with re-exploration and hemostatic sealing agents.

<sup>g</sup> Includes one aneurysm patient with intrapleural hematoma, treated with exploratory thoracotomy and evacuation; one ulcer patient with bleeding and tamponade, treated with intercostal vessel ligation.

<sup>h</sup> One aneurysm patient who developed an aorto-esophageal fistula at follow-up, treated with custom endograft placement.

<sup>i</sup> One aneurysm patient with growth, treated with placement of additional endovascular graft components, who also underwent secondary intervention for growth at 31-365 days, as discussed in note ‘e’.

## H. Clinical Utility

Another secondary hypothesis was superior clinical utility in the endovascular treatment group compared to the open surgical control group. All clinical utility measures were superior in the endovascular treatment group compared to the open surgical control group ( $p < 0.01$ ), as reported in Table 24.

**Table 24. Clinical Utility Measures**

Measure	Endovascular	Open Surgical	Diff (95% CI) <sup>1</sup>	p value <sup>2</sup>
Number of blood transfusions	0.3 ± 1.0 (160)	1.7 ± 1.9 (70)	-1.4 (-1.9, -0.9)	<0.01
Duration of intubation (hrs)	2.8 ± 4.6 (147)	53.1 ± 85.4 (66)	-50 (-71, -29)	<0.01
Duration of ICU stay (days)	2.2 ± 6.2 (153)	9.4 ± 16.9 (70)	-7.2 (-11, -3.1)	<0.01
Days to ambulation	1.6 ± 2.5 (148)	5.5 ± 5.6 (63)	-3.9 (-5.4, -2.5)	<0.01
Days to resumption of oral fluid intake	0.7 ± 1.9 (155)	4.0 ± 5.6 (60)	-3.3 (-4.8, -1.8)	<0.01
Days to resumption of regular diet	1.9 ± 2.7 (156)	5.2 ± 3.7 (58)	-3.3 (-4.4, -2.3)	<0.01
Days to resumption of bowel function	2.9 ± 2.3 (94)	5.5 ± 3.3 (61)	-2.6 (-3.6, -1.7)	<0.01
Days to hospital discharge	5.0 ± 8.6 (159)	16.1 ± 18.7 (70)	-11 (-16, -6.4)	<0.01

<sup>1</sup> Confidence interval on difference in means utilized the T-distribution and is unadjusted for multiplicity.

<sup>2</sup> p values are unadjusted for multiplicity.

## I. Evaluation of Gender Bias

The distribution in gender was not significantly different between study groups, yet, in order to more carefully evaluate possible gender-based differences in outcome of treatment with the Zenith TX2<sup>®</sup> TAA Endovascular Graft, a gender subset analysis was performed on outcomes related to safety and effectiveness. Specifically, the percent of patients with severe morbid events within 30 days and the Kaplan-Meier freedom from device events within 12 months were evaluated.

The analysis showed that the percent of female patients experiencing severe morbid events within 30 days was 2.2% (1/45) in the endovascular treatment group and 28.6% (8/28) in the open surgical control group. Kaplan-Meier freedom from device events at 12 months was 86% for female patients in the endovascular treatment group. The results, as described above, show that the benefits of TAA therapy, in terms of freedom from severe morbidity and freedom from device events, in the female patient subset are consistent with the results of the overall pivotal analysis; additional analyses of the performance of this device in female patients will be conducted as part of the a post-approval study.

## J. Evaluation of Ulcer Patients

Separate analyses were provided for ulcer patients treated during the primary study. A total of 12 institutions enrolled 23 endovascular treatment patients with descending thoracic ulcers. At 12 months, 22 of these patients were eligible for follow-up. Twenty-one (95%) had clinical follow-up and 20 (91%) had CT imaging.

The 30-day and 365-day all-cause mortality survival estimates were 100% for the ulcer patients. The 30-day mean total morbidity score was  $0.6 \pm 1.0$  for ulcer patients, as compared to  $1.3 \pm 3.0$  for the ulcer and aneurysm patients combined. No ulcer patients experienced a

severe morbid event within 30 days of treatment. The 365-day survival estimate of freedom from severe morbid events was 91.1% in this group.

No device integrity issues, migrations, ruptures or conversions were reported for ulcer patients through 730 days. There were no reports of device kink, compression, or loss of patency. Two (2) patients experienced an increase in ulcer depth >5 mm at one or more timepoints; one patient appears to have stabilized. Two patients had an endoleak at pre-discharge; both had resolution without intervention by the time of the 30-day follow-up. One patient had a reported Type III endoleak at the 12-month follow-up; however, the source of the leak is unknown as this patient had a one-piece device placed with no additional components.

The results from the separate analyses show that the results for ulcer patients were within expected limits.

## **XII. PANEL MEETING RECOMMENDATIONS**

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 safety data from the TX2 study showed that 30-day mortality was non-inferior in the endovascular treatment group compared to the open surgical control group. Morbidity at 30 days, as measured by the mean number of pre-specified events per patient, was non-inferior in the endovascular treatment group compared to the open surgical control group. All clinical utility measures were superior in the endovascular treatment group compared to the open surgical control group.

Effectiveness was evaluated as freedom from rupture, with no ruptures in either the endovascular treatment group or open surgical control group. A Kaplan-Meier analysis for freedom from any of the following device events: technical failure; loss of patency; rupture; secondary intervention; conversion; stent fracture; Type I or III endoleak; or migration showed freedom from any device event as 94.9% at 30 days and 90.1% at 365 days. There were also no conversions in the endovascular treatment group. Data beyond 12 months continue to support device safety and effectiveness, and follow-up remains on-going through a post-approval study.

## **XIV. CDRH DECISION**

CDRH issued an approval order on May 21, 2008. The final conditions of approval cited in the approval order are described below. The structure of the PAS protocol was influenced by data developed from the clinical studies, including observed adverse event rates and performance metrics.

- Cook 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 US 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.

- Cook must perform a post-approval study for the Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System to evaluate the longer-term safety and effectiveness of the Zenith® TX2® Thoracic TAA Endovascular 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 any cause occurring within 30 days of the initial procedure or a secondary intervention; or any death determined by the independent clinical events committee to be causally related to the initial implant procedure, secondary intervention, or rupture of the treated aneurysm.

This study is expected to include 273 patients, 160 endovascular patients from the original pivotal study cohort, as well as enrollment of an additional 125 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, blood tests, pulses, ABIs, and a clinical 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. Upon completion of this post-approval study, Cook must provide a supplement with revised labeling that reflects the study findings.

- Cook must perform an evaluation to better understand the overall outcomes in females and non-Caucasians undergoing endovascular aneurysm repair (EVAR) with the Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System. This evaluation will include a subset evaluation of the females and non-Caucasians enrolled in the post-approval study described 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 Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System-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 above.
- Cook must implement a training program, as outlined in the PMA, which includes a subset analysis to examine the skills of new practitioners in the use of the Zenith® TX2® Thoracic TAA Endovascular Graft with the H&LB One-Shot™ Introduction System. This evaluation will include a subset of the 160 patients enrolled in the post-approval study

described in item 2 above. Cook will evaluate a 30-day composite device effectiveness measure of freedom from any one of the following events in up to 5 patients from each site: technical failure; loss of patency (by core lab analysis); rupture; secondary intervention; conversion; stent fracture (by core lab analysis); Type I or III endoleak (by core lab analysis); or migration. 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 SPECIFICATION**

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.