SUMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Endovascular Stent Graft
Device Trade Name:	Aorfix™ AAA Flexible Stent Graft System
Device Product Code:	MIH
Applicant's Name and Address:	Lombard Medical Technologies Inc. 2050 East ASU Circle, Suite 103 Tempe, AZ 85284 USA
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P110032
Date of FDA Notice of Approval:	February 14, 2013
Expedited:	Not applicable

II. INDICATIONS FOR USE

The Aorfix™ AAA Flexible Stent Graft System is indicated for treatment of patients with abdominal aortic and aorto-iliac aneurysms having vascular morphology suitable for endovascular repair, including:

- Adequate iliac or femoral access that is compatible with vascular access techniques, implants, and accessories.
- Aortic neck landing zone diameters with a range of 19mm to 29mm.
- Non aneurysmal proximal neck center-line length of $\geq$ 15mm.
- Infrarenal aortic neck angulations including those up to and including 90°.
- Common iliac landing zone diameters with a range of 9mm to 19mm.
- Distal fixation length of $\geq$ 15mm.

III. CONTRAINDICATIONS

The Aorfix™ AAA Flexible Stent Graft System is contraindicated in:

- Patients who have a condition that threatens to infect the graft.
- Patients with known allergies or sensitivities to the implant materials (including polyester, Nitinol and tantalum).

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Aorfix™ AAA Flexible Stent graft System labeling.

V. DEVICE DESCRIPTION

The Aorfix™ AAA Flexible Stent Graft System is an endovascular stent graft system for treating infra-renal aortic and aorto-iliac aneurysms. When placed within the aneurysm, the Aorfix™ AAA Flexible Stent Graft System creates an internal bypass of the aneurysm to reduce the risk of rupture.

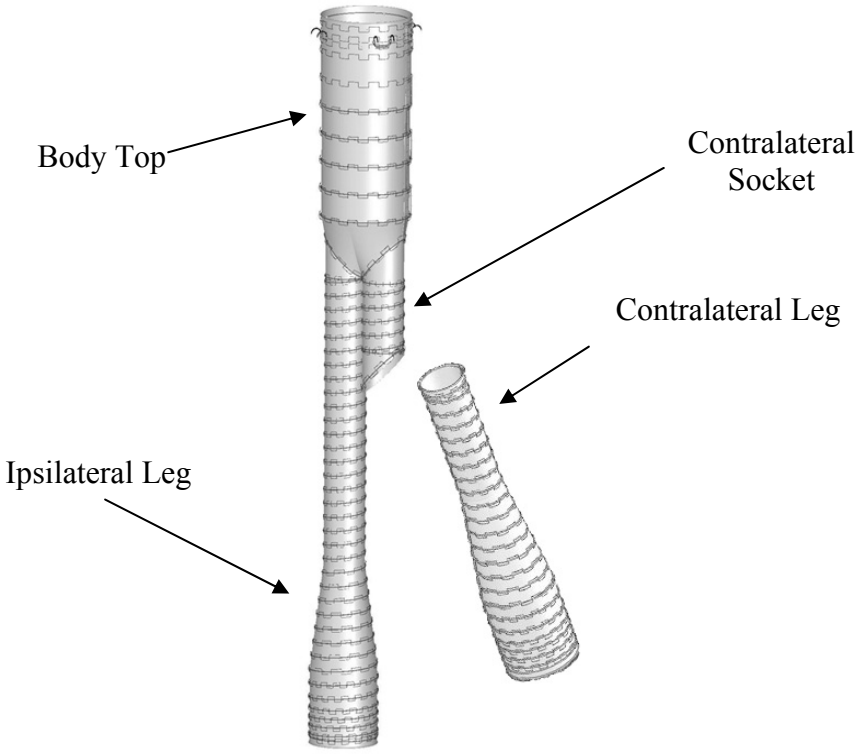
The Aorfix™ AAA Flexible Stent Graft System is a modular system where each component comprises: an implantable stent graft (Aorfix™ Stent Graft) and a disposable delivery system (Aorfix™ Delivery System). The stent graft is a two-piece system consisting of 1) a main body incorporating an ipsilateral leg component and a contralateral socket and 2) a contralateral plug-in leg. The main body has four sets of hooks positioned at the proximal end to aid fixation. The contralateral socket is a standard 12mm diameter component, with an oblique distal end that is designed to assist cannulation with a guide-wire. Radiopaque markers made of tantalum wire rings are located at the open ends of graft components. A bifurcated main body implant, with contralateral leg, is shown in Figure 1.

Distal and proximal extension stent graft implants are available and may be used as required. For bailout, an aorto-uni-iliac (AUI) converter is also available. The delivery systems for the proximal extender and AUI converter are the same as the main body delivery system while the delivery systems for the distal extenders are the same as the contralateral leg delivery system.

Each implant has a dedicated delivery system (22Fr main body and 20Fr contralateral leg). The delivery systems are designed to provide accurate placement of each implant and can be used by a single operator. See Instructions for Use (IFU) for the full range of sizes for the aortic body, ipsilateral limb, contralateral leg, iliac and proximal extensions, and AUI converter.

Nitinol (nickel / titanium alloy) is used for all stent and hook components, tantalum is used for all radiopaque markers and polyester is used for the graft and suture materials.

Figure 1 Bifurcated Main Body of Graft with Contralateral Leg



A. Main Body

The main body stent graft has three sections – the body top, the ipsilateral leg and the contralateral socket as described below. It is available with proximal diameters from 24mm to 31mm.

The key features of the body top are shown in Figure 2. Four pairs of hooks are positioned circumferentially 90° apart at the proximal end and are designed to resist migration. The reinforcing wire is in ring form, rather than a traditional zig-zag or diamond mesh stent. At the proximal end, the wire rings are placed closer together than in the body to increase radial force and they are also placed on the inside of the graft to improve the seal between the graft and the vessel wall. There is a radiopaque ring around the top of the device.

Figure 2 Main Body Hooks

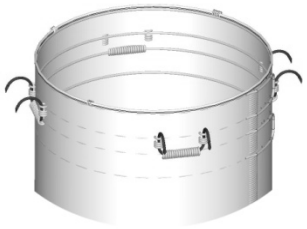


Figure 3 shows that the reinforcing wire in the main body is continuous and, between stent rings, the wire is bent to run longitudinally in an offset, stepwise fashion. The longitudinal parts of the wire run in the seam of the device.

Note that when implanted, the stent graft rings are deformed to have a saddle or 'fishmouth' shape, also shown in Figure 3 and photographed in Figure 4.

This shape allows the stent graft to be placed trans-renally, with the fishmouth trough aligned with the renal arteries juxtarenally and the fishmouth peak extending suprarenally. Note that the seam referred to above is part of the fishmouth peak. The seam is less flexible than the rest of the graft and, in curved vessels, placing the seam on the inner curve should be avoided. This requirement and the orientation of the seam to the fishmouth are usually met by placing the device with the seam anteriorly in the patient with exact alignment determined by the orientation of the renal arteries. To aid this orientation, there is a longitudinal radiopaque wire running within the seam of the main body.

Figure 3 Shape of Nitinol Wire Used to Form Stent Rings

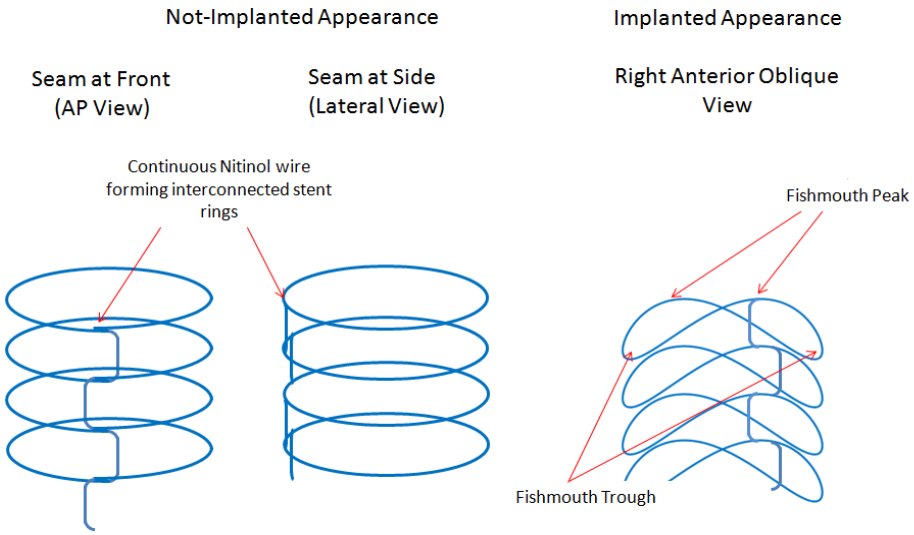


Figure 4 Lateral View of Stent Graft Once Deployed, Showing the Fishmouth Shape.

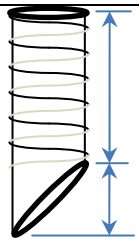
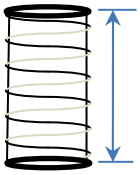
B. Ipsilateral Leg

All ipsilateral legs have a standard 12mm internal diameter at their proximal ends. The distal ends are flared on legs with distal diameters larger than12mm and taper down for the 10mm distal diameter. The range of sizes for the distal diameter of this implant is from 10mm to 20mm in 2mm steps. There are no hooks on the leg. All leg components in the Aorfix™ AAA Flexible Stent Graft System are reinforced with Nitinol wire that is wound in a continuous helical shape.

C. Contralateral Socket

The socket also has a standard 12mm internal diameter and has an oblique distal end. There is a proximal radiopaque wire ring as well as the distal radiopaque ring to provide a visual guide to the physician when cannulating the contralateral socket. Note that the oblique entrance to the contralateral socket is not present in the 81mm long main body implant.

Figure 5 Contralateral Sockets

	
Contralateral Socket used on Body lengths: 96mm, 111mm, 128mm, 142mm	Contralateral Socket used on Body length: 81mm

D. Contralateral (Plug-In) Leg

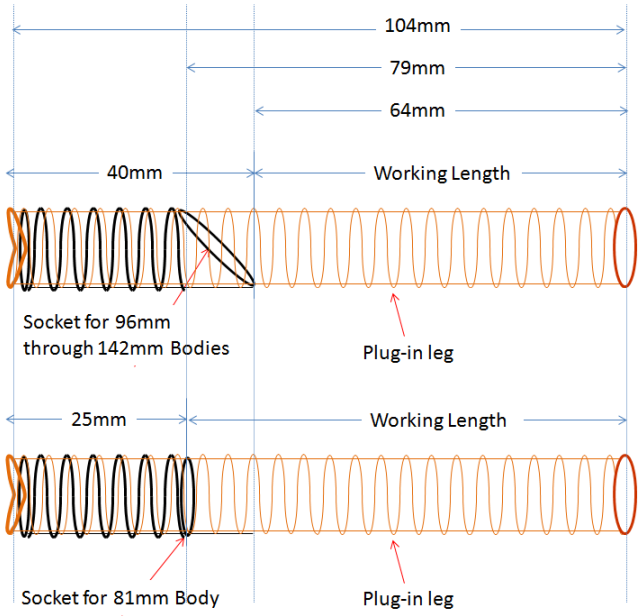
All contralateral legs have a standard 12mm internal diameter at their proximal ends. The distal ends are flared on legs with distal diameters larger than12mm and taper down for the 10mm distal diameter. The range of sizes for the distal diameter of this implant is from 10mm to 20mm in 2mm steps. There are no hooks on the leg.

The specified length of the leg is the Working Length and is the length of implant that projects beyond the contralateral socket; the actual length of the implant is 40mm longer than the working length to provide for full over-lap in the socket.

Note: When using the 81mm body, the socket is 15mm shorter than on all other body lengths, making the Working Length of the contralateral legs 15mm longer (See Figure 5 and Figure 6). For example, Figure 6 shows a 64mm contralateral leg. Its overall length is 104mm and it has a Working Length of 64mm when plugged into a 40mm socket. This socket is found on all main body grafts apart from the 81mm graft. This shortest graft has a 25mm socket and this has the effect of increasing the working length of the contralateral leg to 79mm.

The working length for both socket sizes is indicated on the box label for contralateral legs.

Figure 6 Dimensions of a Contralateral plug in leg



E. Proximal and Distal Extender Components

All extension pieces (shown in Figure 7) have the same diameter at both ends and have radiopaque wire rings at the proximal and distal openings to aid visualization.

Like the main body, the proximal extension pieces have hooks at the proximal end, the same design of Nitinol rings, and radiopaque wire along the seam. They are available in diameters 24mm through 31mm. Shown in Figure 8, the proximal extender also has a fishmouth shape which should be deployed with the same orientation as the fishmouth of the main body.

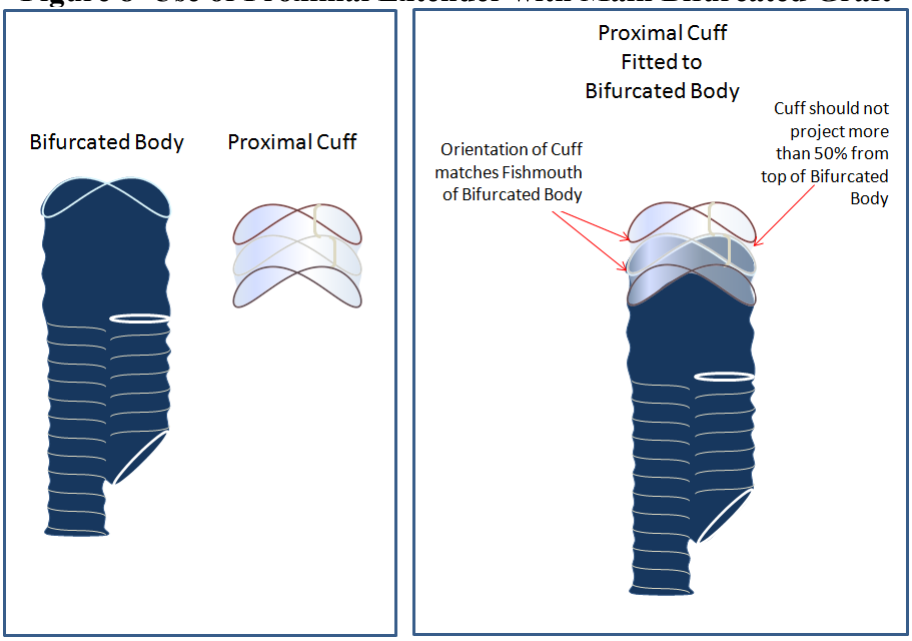
The distal extender has the same construction as the leg components using helical wound Nitinol wire. It is available in diameters 10mm through 20mm.

Figure 7 Proximal and Distal Extension Pieces

Proximal Extender

Distal Extender

Figure 8 Use of Proximal Extender with Main Bifurcated Graft



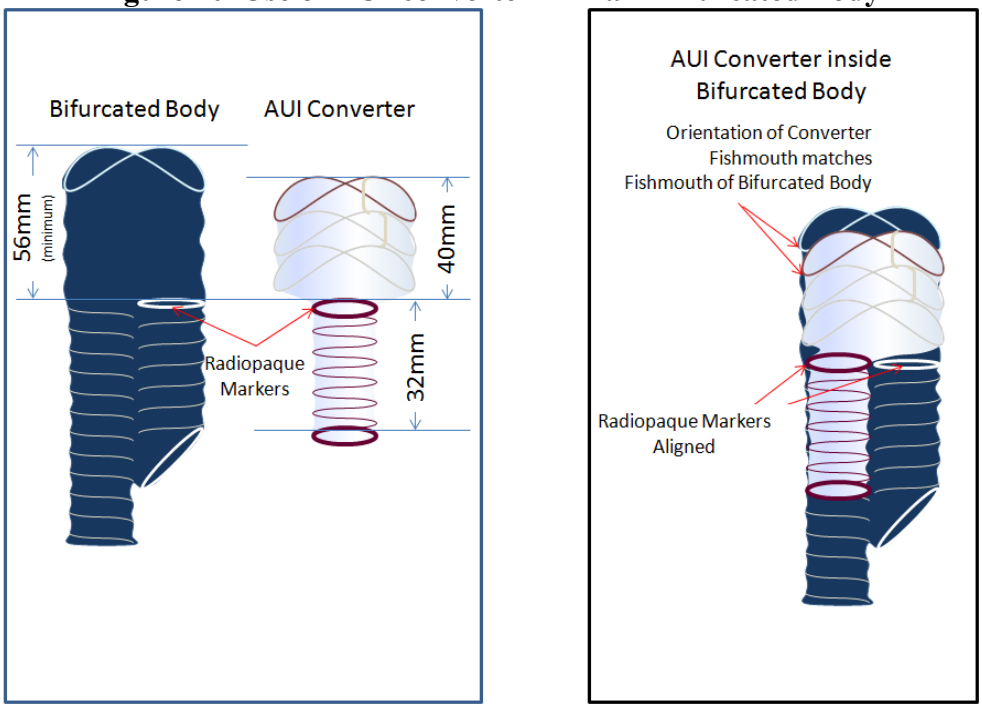
F. Aorto-Uni-Iliac Converter (AUI Converter)

The AUI converter (Figure 9) is for use as a 'bail-out' device in procedures where it has not been possible to gain access for the contralateral delivery system to the contralateral gate. Like the main body, the AUI converter consists of a body component and a leg component. The AUI converter body component is fabricated in the same way as the body component for the main body of the primary graft, and the leg component of the AUI converter is fabricated in the same way as the ipsilateral leg component. The AUI converter is designed to fit on the flow divider of the Aorfix™ main body and it has a fishmouth which should have the same orientation as the primary graft. Proximal diameters are 25mm, 27mm, 29mm and 31mm. Converters are designed to use the same size as, or 1mm larger than, the aortic diameter of the primary graft.

Figure 9 AUI converter

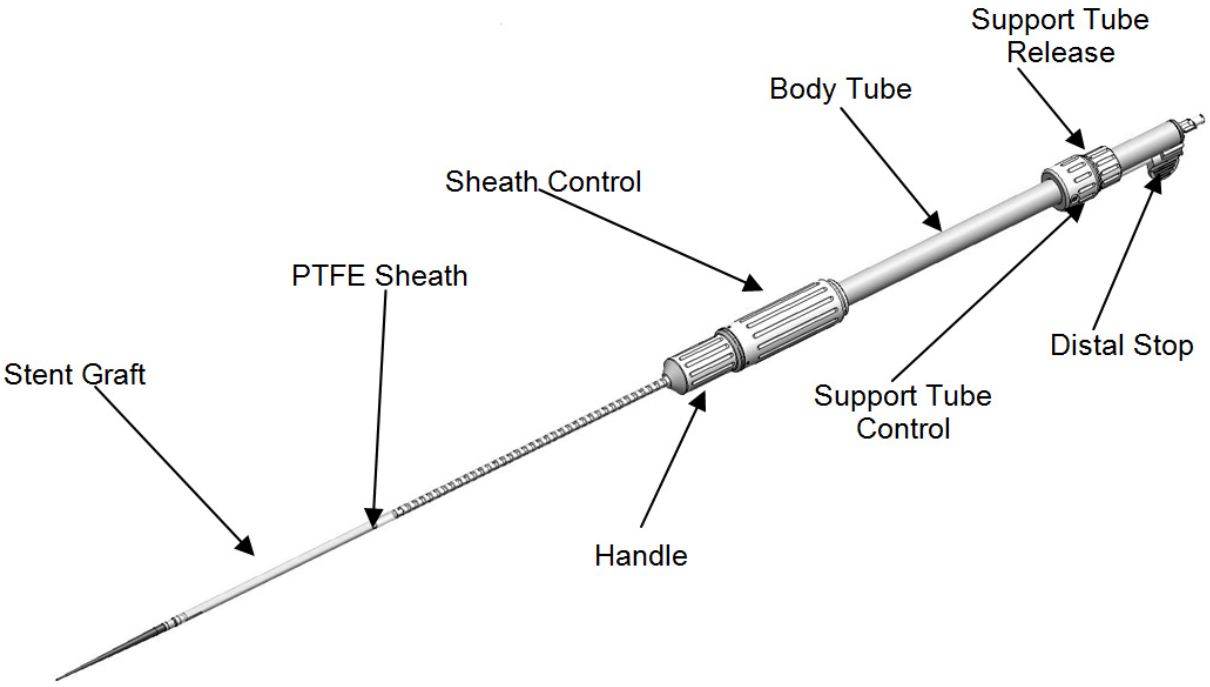
Figure 10 illustrates correct position of the AUI converter in the main body graft. The top of the AUI converter leg should be aligned with the flow divider in the main body, the top of the converter should be below the top of the main graft and, in order to avoid inadvertent coverage of the renal arteries, the fishmouth at the top of the AUI converter should have the same orientation as the fishmouth of the main body graft.

Figure 10 Use of AUI converter in Main Bifurcated Body



G. Aorfix™ AAA Flexible Stent Graft System Main Body Delivery System

Figure 11 Main Body Delivery System



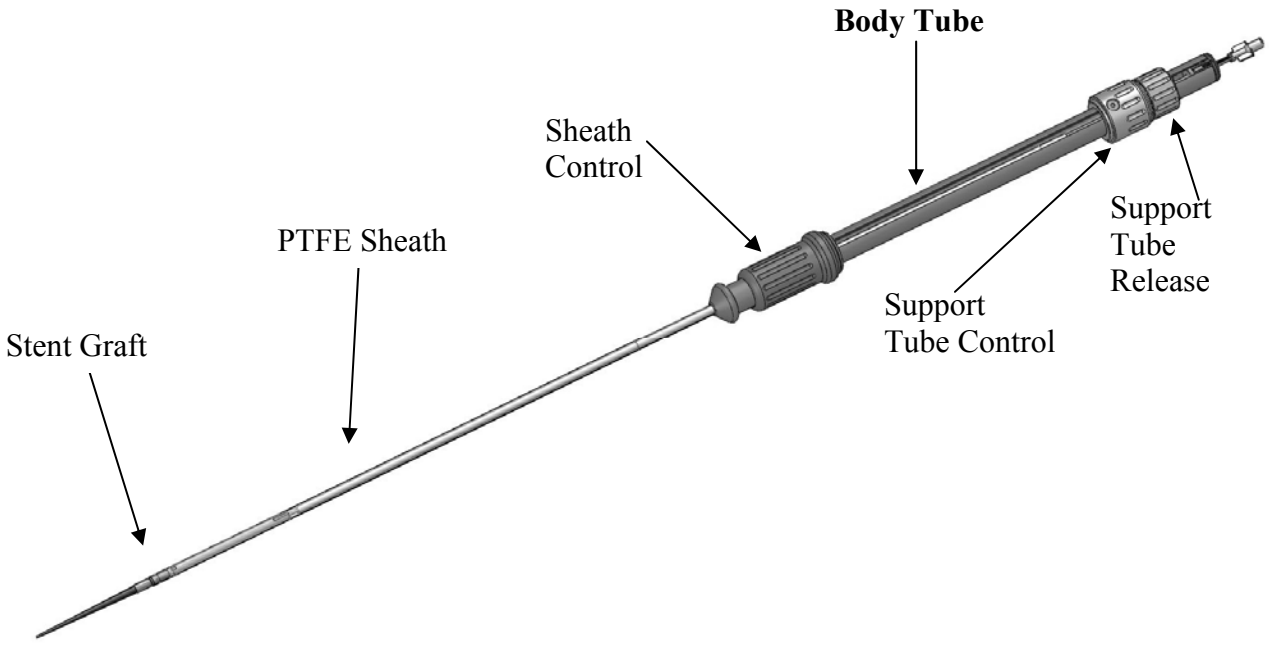
The main components of the Aorfix™ AAA Flexible Stent Graft System delivery system are shown above and are listed below in Table 1. The delivery system is operated by the sheath control which pulls the sheath back to deploy the stent graft. The control is rotated counter-clockwise while the fishmouth is being positioned. There is a ratchet which clicks while the control is being rotated. At the end of the ratchet, the Sheath Control spins freely at which point the mouth of the graft will have been fully deployed. The rest of the graft is deployed by pulling the sheath control distally.

Table 1 Components of the Main Body Delivery System

Part	Description
Stent Graft	The stent graft is compressed within the sheath. Its proximal and distal ends can be clearly seen, as well as the entrance to the contralateral gate which is a plain white oval of fabric midway down the graft.
PTFE Sheath	The PTFE sheath has a 22Fr Diameter and contains the stent graft and attachments to it. The sheath is translucent and allows the key parts of the stent graft to be seen through it.
Handle	The handle is firmly attached to and stabilizes the body tube while the sheath control and support tube controls are adjusted.
Sheath Control	This control retracts the sheath in two stages; stage one uses a counterclockwise screw thread to release the proximal end slowly and stage two uses a simple pull back to deploy the rest of the graft.
Body Tube	This is a blue colored tube that is attached to the handle and which carries all the controls of the deployment mechanism. When the seam on the main body graft is anterior, a full length slot in the body tube should face towards the patient.
Support Tube Control	This control was initially intended to aid dilation of the mouth of the graft but was found to be ineffective in highly angled necks. It is recommended that the control is not used during deployment.
Support Tube Release	This control disconnects the support tubes from the proximal end of the stent graft.
Distal Stop	This clip prevents the support tube controls from moving during deployment. It must be removed before operating the support tube release.

H. Contralateral Delivery System

Figure 12 Contralateral Leg Delivery System



When the proximal end of the contralateral plug-in leg (Figure 12) is aligned with the proximal radiopaque marker on the contralateral socket of the main body, the sheath control is moved directly back, i.e. without a twisting action, to deploy the implant. Once the contralateral leg is fully deployed, the support tube release is detached from the support tube control to release the implant. The delivery system is then withdrawn.

Table 2 lists all components of the contralateral delivery system.

Table 2 Components of the Contralateral Delivery System

Part	Description
Stent Graft	The stent graft is compressed within the sheath. Its proximal and distal ends can be clearly seen.
PTFE Sheath	The PTFE sheath has a 20Fr Diameter and contains the stent graft and attachments to it. The sheath is translucent and allows the key parts of the stent graft to be seen through it.
Sheath Control	This control pulls the sheath back to deploy the stent graft. The stent graft is deployed by pulling the sheath control distally.
Body Tube	This is a blue colored tube that is attached to the handle and which carries all the controls of the deployment mechanism.
Support Tube Control	This control is locked and inoperable on this delivery system.
Support Tube Release	This control disconnects the support tubes from the proximal end of the stent graft.

I. Ancillary Components Delivery System

The proximal extender and AUI converter have the same delivery system as the main body implant. Distal extender pieces have the same delivery system as the contralateral leg.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are three primary alternatives to using the Aorfix™ AAA Flexible Stent Graft System for the correction of abdominal aortic aneurysms (AAA). These include: endovascular repair using a commercially available endovascular grafting system (note: currently, not all endovascular grafting systems are approved in the US for treating necks angled more than 60°); 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

The Aorfix™ AAA Flexible Stent Graft System has been commercially available outside the United States since March 2006 and is currently available in the following countries: Argentina, Austria, Brazil, Cyprus, Czech Republic, Germany, Great Britain, Greece, Hungary, Ireland, Italy, Netherlands, Poland, Russia, Slovakia, Slovenia, Spain, Sweden, Turkey and Uruguay. It has never been withdrawn from any market as a result of risk of serious adverse health consequences.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Insertion and other vascular access site complications for example infection, dissection, bleeding, pain, delayed healing, hematoma, dehiscence, seroma, cellulitis, nerve injury/damage, arteriovenous fistula;
- Allergic reaction and/or anaphylactic response for example to x–ray contrast dye, anti-platelet therapy, device materials;
- Anesthetic complications and subsequent attendant problems;
- Blood or bleeding events for example hemorrhage, anemia, gastrointestinal bleeding, coagulopathy;
- Bowel events for example bowel ischemia, paralytic or adynamic ileus, obstruction, fistulae;
- Cardiac events consequent to general anesthesia and abdominal surgery and, for example, transient aortic occlusion during ballooning;
- Death;
- Loss of stent graft function arising from, for example, improper component placement or deployment, component migration, occlusion, infection, loss of integrity requiring surgical revision, perforation and endoleak;
- Embolic and thrombotic events (with transient or permanent ischemia or infarction), for example, deep vein thrombosis, renal embolism, micro embolic shower;
- Arterial fistulae with, for example, vein, lymphatic, bowel;
- Infection, for example urinary tract, systemic or localized, endograft, sepsis;
- Generalized inflammatory response, for example, elevated temperature (post implantation syndrome);
- Ischemic losses arising from, for example, planned or inadvertent occlusion of branch vessels including complications to systems such as: hepatic, gastric, splenic, bowel, neurologic, genitourinary and musculoskeletal;
- Hepatic failure;
- Lymphatic complications and subsequent attendant problems, for example, lymphocele, lymphatic fistula;
- Multi-system organ failure;
- Neurologic or cerebral events and subsequent attendant problems, for example, transient ischemic attacks, cerebrovascular accident (hemorrhagic or embolic), reversible ischemic neurologic deficit, nerve injury, paraparesis and paraplegia;
- Pulmonary events consequent to general anesthesia and abdominal surgery;
- Renal complications, for example, acute and chronic renal failure, renal microembolism, renal insufficiency, renal artery occlusion, contrast toxicity;
- Endovascular or surgical reintervention to correct deficit caused by, or loss of performance of, stent graft including surgical conversion to open repair;
- Impotence/ sexual dysfunction;
- Shock;
- Vessel damage, for example, dissection, plaque disruption, rupture, thrombosis, occlusion and fistulae.

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

IX. SUMMARY OF PRECLINICAL STUDIES

Lombard Medical completed comprehensive biocompatibility (Section A), in vitro bench and analytical testing (Section B), animal studies (Section C), and Sterility, Packaging and Shelf Life testing (Section D) on the Aorfix™ AAA Flexible Stent Graft System to support the safety and effectiveness of the device. The testing included the stent graft, iliac limbs, extensions and delivery system following recognized standards and guidance documents.

A. Biocompatibility

Biocompatibility testing was conducted on the Aorfix™ AAA Flexible Stent Graft System to ensure that the finished device is safe and biocompatible. Testing was performed in accordance with ISO 10993-1. The Aorfix™ Stent Graft was categorized as an implant device with permanent blood contact (>30 days). The Aorfix™ Delivery System was categorized as an external communicating device in limited contact with circulating blood (<24 hours).

All testing performed met the requirements as specified within the applicable standard.

Table 3 Biocompatability Testing

Test	What Tested	Method	Purpose	Results
*S. typhimurium** Reverse Mutation Assay (Ames)	Implant	Extracting Media: A) 0.9% sodium chloride B) DMSO Conditions: 70°C / 24 hours	Evaluate the potential of the test article to induce reverse mutations in five strains of Salmonella typhimurium in the presence and absence of exogenous mammalian metabolic activation system (S-9)	Pass Non-Mutagenic Test article extracts did not produce a two-fold increase in the number of revertants in any of the 5 extracts.
Mouse Lymphoma*	Implant	Extracting Media: A) 0.9% sodium chloride injection USP B) DMSO Conditions: 70°C / 24 hours	Determine the ability of the stent graft to induce forward mutations at the thymidine kinase (TK) locus as assayed by colony growth of L5178Y mouse lymphoma cells in the presence of trifluorothymidine (TFT)	Pass Non-Mutagenic None of the test article treatments induced substantial increases in the number of revertant colonies.
In vitro Chromosomal Aberration*	Implant	Extracting Media: A) Physiological Saline B) DMSO Conditions: 70°C / 24 hours	Determine whether the test article extract causes genotoxicity in Chinese hamster ovary cells	Pass Non-genotoxic
ISO Implant test*	Implant	New Zealand White Rabbits Test articles implanted 2.5-5cm from midline, parallel to spinal column about 2.5cm apart. Control articles implanted in same manner on other side of spinal column. Control: USP Reference Standard HDPE (1x10mm)	Evaluate the potential of the test article to induce irritancy effects after implantation in muscle tissue of rabbits for 7, 30, 90 and 365 days	Acceptable No gross evidence of local irritancy
ISO Dog Thrombogenicity	Implant and functional end of delivery system	Two purebred female beagles Test article surgically inserted into jugular vein. The control article was inserted into the opposing jugular vein of the test subject. Control article: Negative Control	Evaluate the potential of the test article to resist thrombus formation when placed in the vasculature of dogs	Acceptable The amount of thrombosis formed was not considered significant and was comparable to negative control.

Test	What Tested	Method	Purpose	Results
		Plastic (ex Toxikon) Implantation time of 4 ± 1/2hrs		
Complement Activation Assay, C3a and SC5b-9	Implant and functional end of delivery system	Extraction Media: NaCl Conditions: 37°C for 72 hours. Test then exposed to plasma and incubated at 37°C for 90 minutes prior to assaying for complement proteins.	Measure complement activation in human plasma as a result of exposure of the plasma to the test article	Acceptable Concentration of C3a and SC5b-9 in the test extract was not significantly greater as compared to both negative and plasma controls.
ISO MEM Elution	Implant and functional end of delivery system	Extracting Media: MEM Conditions: 37°C / 24 hours	Evaluate cytotoxic effects of the test article on a mouse fibroblast monolayer	Pass Non-cytotoxic
Murine Local Node Assay	Implant and functional end of delivery system	Extracting Media: A) 0.9% sodium chloride injection USP B) acetone in olive oil Conditions: 70°C / 24 hours or 50°C /72hrs	Evaluate the allergenic potential or sensitizing capacity of the test article	Pass No evidence of sensitization
ISO Intracutaneous Reactivity	Implant and functional end of delivery system	Extracting Media: A) 0.9% sodium chloride injection USP B) cottonseed oil (OIL) Conditions: 70°C / 24 hours or 50°C /72hrs	Evaluation of irritation or toxic effects of leachables extracted from the test articles in rabbits	Pass Non- irritant
USP Systemic Injection Test	Implant and functional end of delivery system	Extracting Media: A) sodium chloride injection USP (IV administered) B) cottonseed oil (IP administered) Conditions: 70°C / 24 hours or 50°C /72hrs	Evaluate the test article for potential toxic effects after single dose injection into mice	Pass Non-toxic
Hemolysis – direct contact method	Implant and functional end of delivery system	Negative Control: 0.9% sodium chloride injection USP Positive Control: 0.1% sodium carbonate solution Conditions: Incubation in rabbit blood	Evaluate hemolytic activity of the test article in rabbits	Pass Non-hemolytic

Test	What Tested	Method	Purpose	Results
		at 37°C for 60 minutes		
Partial Thromboplastin Time (PTT)	Implant and functional end of delivery system	Negative Control: Human plasma Positive Control: Crushed glass beads 0.4g/2.0ml Conditions: Incubation in plasma at room temperature for 60minutes. 0.2ml aliquots were incubated at 37°C for 60secs. 0.2ml PTT reagent was added and samples incubated for exactly 3mins before clotting induced.	Measure the effect of the test article on clotting time of human plasma	Acceptable Difference between test sample and negative control = 3 seconds, difference between test sample and positive control = 30 seconds
Prothrombin Time (PT)	Implant and functional end of delivery system	Negative Control: Human plasma Positive Control: Acculot™ Control II Incubation in plasma at room temperature for 60minutes. 0.2ml aliquots were incubated at 37°C for 3-4minutes before clotting induced.	To measure the effect of the test article on clotting time of human plasma	Acceptable Test sample demonstrated a similar clotting time when compared to the negative control.

B. Laboratory Studies

1. Bench Testing

Lombard conducted bench testing on the Aorfix™ AAA Flexible Stent Graft System including both the stent graft and the delivery system. All testing was conducted in accordance with national and international standards and guidance documents, primarily EN 12006-3 (Non-active surgical implants – particular requirements for cardiac and vascular implants. Endovascular Devices), ISO 7198 (Cardiovascular implants – Tubular vascular prostheses) and ISO 25539-1 (Cardiovascular Implants. Endovascular devices. Endovascular Prosthesis). The testing details include results from T=0 (baseline, no ageing) as well as results using samples accelerated aged to 2 years (T=2). Testing verified that the Aorfix™ AAA Flexible Stent Graft System (implant and delivery systems) met its product performance and design specifications.

Results obtained from *in vitro* testing provided evidence supporting the safety and effectiveness of the Aorfix™ AAA Flexible Stent Graft System, see Table 4.

Table 4 Bench Testing Summary

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
Dimensional Verification and Component Dimension Compatibility*	(72) Main Body (72) Leg	Dimensional Verification: Maximum effective length (handle to tip) for: A5-22 Delivery System is 595mm maximum. A6-20 Delivery System is 555mm maximum.	Dimensional Verification: All samples met acceptance criteria.
		Dimensional Compatibility: Guide-wire to pass completely through the central lumen of the delivery system without any impediment.	Dimensional Compatibility: All samples met acceptance criteria.
		Luer lock mating connector to indicate acceptable function.	All samples met acceptance criteria.
Profile/ Diameter Test*	(72) Main Body (72) Leg	*Profile* – The diameter of the effective length for: A5-22 Delivery System is 7.6mm ±0.2mm. A6-20 Delivery System is 6.6mm ±0.2mm.	The profile of the effective length was found to be acceptable for clinical use.
Assessment of Haemostasis*	(33) Main Body (33) Leg	Leakage from the test delivery systems must be $\leq 10 cm^3$/minute in all cases.	The leakage from the delivery system was found to be acceptable for clinical use.
Simulated Use Models*	(22) Main Body (22) Leg	The tester must be in agreement with all statements listed below:	Testing was carried out in a pulsatile flow model with tortuous iliacs and a highly angulated neck.

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
		Pushability: The delivery system is able to advance into position in the anatomical model without bending or buckling.	Results of the testing were found to be sufficient for clinical use.
		Torquability: The delivery system handle transmits sufficient rotational rigidity to the implant end of the catheter.	Results of the testing were found to be sufficient for clinical use.
		Trackability: The delivery system is able to advance over the guide wire, following the guidewire tip, along the path of the vessel.	Results of the testing were found to be sufficient for clinical use.
		Flex/Kink: The delivery system and implant are able to bend in order to accommodate the minimum radius or angle negotiated during access and delivery.	Results of the testing were found to be sufficient for clinical use.
		Ability to access the intended deployment site: The delivery system enables access to the deployment site.	Results of the testing were found to be sufficient for clinical use.
		Deployment accuracy: Stent Graft Body: At its closest, the proximal wire rung is less than 7mm from the left renal artery marker. The implant has not occluded the target renal artery marker. Proximal Extender: The HPE implant successfully extended the stent graft body implant. Contralateral Leg: The HBL implant was successfully positioned in the stent graft body implant.	Stent Graft Body: Results of the testing were found to be sufficient for clinical use. Proximal Extender: Results of the testing were found to be sufficient for clinical use. Contralateral Leg: Results of the testing were found to be sufficient for clinical use.

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
		Visual inspection of deployed prosthesis: The implant maintains adequate contact with the vessel wall. There are no unacceptable kinks, bends, or twists. There is no unacceptable component separation between modular implant or components of the implant.	Results of the testing were found to be sufficient for clinical use.
		Ability to deploy: The delivery system enables the user to deploy the implant as intended.	Results of the testing were found to be sufficient for clinical use.
		Ability to withdraw: The delivery system is able to be successfully withdrawn.	Results of the testing were found to be sufficient for clinical use.
		Condition of delivery system: The delivery system is in an acceptable condition i.e. all joints are intact and there is no material damage that could cause harm to a subject.	Results of the testing were found to be sufficient for clinical use.
		Final statements: The delivery system can successfully deploy the stent graft as described in the IFU. The delivery systems, implants and ancillary implants were all compatible when used in accordance with the IFU. The process is practical for use in operating conditions. The expanded implant (when used with other implant modules) is patent and excludes the aneurysm.	Results of the testing were found to be sufficient for clinical use.
Visibility	(6) Main Body	Characterization Study.	The radiopaque markers on the delivery system and implant were evaluated under fluoroscopy. The results indicate that the radiopacity of the delivery system and implant were found to be sufficient for clinical use.

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
Force to Deploy*	(17) Main Body (17) Leg (11) Distal Extender	Characterization Study.	All stent grafts were successfully deployed. The unsheathing force did not exceed the minimum tensile strength of the sheath tubing.
Bond strength / Torsional Bond Strength*	(64) Each joint	Varies depending upon specific test (Acceptance criteria ranged from 15N to 180N tensile and 4.84cNm torsional).	All joints met the pass criteria.
Tip Connector to Center Tube Joint*	(32) Joints	Minimum joint strength 70N.	All samples met pass criteria.
Tubing Longitudinal Tensile Strength	(64) 22Fr (64) 20Fr	22Fr Outer Sheath Material. All Samples >115N at 10% Offset Yield. 20Fr Outer Sheath Material. All Samples >77N at 10% Offset Yield.	All samples met pass criteria.
Dimensional Verification (implant)*	(72) Main Body (72) Leg	All implant dimensions within the defined tolerances.	All samples met pass criteria.
Integral Water permeability/ leakage*	(22) Main Body (22) Leg	Characterization Study.	Stent graft permeability testing was characterized to evaluate the rate of water flow through the Aorfix™ stent graft under pressure of 120mmHg. The mean rate of leakage was 551ml/cm^2/min.
Circumferential Strength*	(22) Main Body (22) Leg	Characterization Study.	The minimum circumferential strength was determined to be 9N/mm, which corresponds to 4366mmHg blood pressure. The failure mode in each case was a graft fabric tear adjacent to the seam. These results demonstrate the circumferential strength of the Aorfix™ stent graft is adequate for the intended clinical use.
Flex Kink*	(17) Main Body (17) Leg (22) Distal Extender	Characterization Study	It was determined that patency was maintained at a radius of curvature of 4mm. Results of the testing were found to be sufficient for clinical use demonstrating the ability of the stent graft to maintain an open lumen in tortuous anatomy.

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
Longitudinal Tensile Strength (implant)*	(17) Main Body (17) Leg (11) Distal Extender	Characterization Study	Mean values for Longitudinal Tensile Strength are as follows: Main Body: 241.8N Leg: 224.7N Distal extender:203.14N The failure mode in each case was fabric tear in the smallest diameter region of the implant. The longitudinal tensile strength is sufficient to ensure the integrity of the implant is maintained in clinical use.
Migration Resistance	(10) Main Body	Characterization Study	The testing characterized the ability of the bifurcated stent graft to resist migration. The peak force required to displace the proximal section of the bifurcated stent graft ranged from 16.47N to 22.66N. The migration resistance is higher than anticipated hemodynamic forces of 8.8N for a 29mm vessel, mean blood pressure 100mmHg.
Migration Resistance	(18) Distal Extenders covering range.	Characterization Study	The testing characterized the ability of the distal extender devices to resist migration. The average force to displace a distal extender across the size range (10mm – 20mm diameter) is 6.7N.
Pull Test for Modular Components* Leg devices	(11) Main Body (11) Leg	Characterization Study	The mean pull out force for modular components (plug-in leg) was 25.15N, which corresponds to a calculated blood pressure of 1668mmHg. Results of the testing are therefore sufficient for clinical use.

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
Pull Test for Modular Components. Distal Extender	(19) Distal Extender	Characterization Study	The mean pull out force for modular components (distal extender) was 11.16 – 36.02N across the range, which corresponds to a minimum calculated blood pressure of 266mmHg. Results of the testing are therefore sufficient for clinical use.
Pull Test for Modular Components. Proximal Extender	(12) Proximal Extender	Characterization Study The proximal extender is intended to provide an adjunctive seal to the primary graft. It is not intended to resist migration forces on the primary graft, which has ts own fixation.	The mean pull out force for modular components (proximal extender) was 7.24N, which corresponds to a minimum calculated blood pressure of 82mmHg. In clinical use fixation of the primary implant is adequate to resist migration. The Proximal Extender is used to extend the sealing zone of the primary implant.
Radial Force	(11) Main Body	Characterization Study	Main body: 30% over-sizing: 1.49N 10% over-sizing 0.43N Distal leg: 20% over-sizing: 1.42N 1 mm over-sizing: 0.21N This testing demonstrates the ability of the Aorfix™ stent graft to exert an outward non-zero radial force, allowing the graft to expand, provide an adequate seal and maintain an open lumen.
Strength of graft to stent bond*	(33) Helical construction (33) Ladder construction	Characterization Study	The mean force to break a single suture is 27.1N The forces necessary to break the sutures are higher than the whole graft migratory forces that the graft will be subjected to in clinical use.
Strength of attachment system bond	(11) Helical construction (11) Ladder construction	Characterization Study	The mean force to initiate separation of the hook is 52.9N The forces necessary to detach the hooks are higher than the whole graft migratory forces that the graft will be subjected to in clinical use.

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
Corrosion Assessment	(6) Main Body (6) Leg	Equivalent or better corrosion behavior when compared to a legally marketed device.	Results of the testing were found to be sufficient for clinical use.
Fatigue and Durability Test (Pulsatile) Whole implant, full physiological simulation.	(8) Main Body, 24mm diameter with (8)Legs plugged into Main Bodies (8) Main Body, 31mm diameter with (8)Legs plugged into Main Bodies	Testing to identify evidence of macroscopic damage that would compromise its functional integrity as indicated in the failure modes identified in the risk analysis.	All devices successfully completed 400,000,000 test cycles. There was no visible deterioration of the devices. Independent examination concluded that the integrity of all devices was maintained. No unexpected failure modes were observed.
90° Neck Angle Fatigue and Durability Test (Pulsatile) Whole implant, full physiological simulation.	(8) Main Body	The test article must not exhibit evidence of macroscopic damage that would compromise its functional integrity as indicated in the failure modes identified in the risk analysis.	All devices successfully completed 400,000,000 test cycles. All samples met the acceptance criteria. The test articles did not exhibit any evidence of macroscopic damage that would compromise the implants' functional integrity as indicated in the failure modes identified in the risk analysis. There was no evidence of any of the following failure modes which would compromise the functional integrity of the implant. • Wire failure in the proximal seal zone. • Wire break / Wire Erosion. • Implant migration. • Fabric wear. • Seam Failure. • Suture Break.

Test	Samples Tested	Specification / acceptance criteria	Summary Test results
Stress Strain Analyses (e.g., Finite Element Analysis)	24mm and 31mm devices plus the helical leg construction which is representative of the Aorfix™ AAA Flexible Stent Graft System	Characterization Study Finite element models of segments of a range of device diameters and pitch were selected to assess the sensitivity of the key design parameters to • manufacturing processes • simulated deployment • cyclical fatigue loading	Within the limits of FEA: • All configurations considered are satisfactory under the uniform radial fatigue conditions. • All configurations have adequate margins of safety, with the larger factors of safety occurring in the larger diameter device segments.
MRI	(6) Main Body (6) Leg	The outcome of the testing provided the recommended scan settings for use with the device. These conditions are included in the device labeling.	The device has been determined to be MR conditional when scanned under the recommended conditions.

(*) Indicates testing was performed at both T=0 and/or T=2.

C. Animal Studies

Two preclinical *in vivo* animal studies were conducted, 1 ovine (12 animals) and 1 bovine (8 animals), using adaptations of the final device design. The ovine animal model required that human sized grafts be scaled to fit the smaller vessels of a sheep. The ovine stent grafts used Aorfix™ AAA Flexible Stent Graft System graft material. Narrower gauge Nitinol wire was used and the wire diameter and spacing of adjacent rings was scaled in proportion to the diameter of the vessel being treated. Hooks were reduced in width from the clinical design to fit onto the smaller implant. All Nitinol wire was treated using the same processes as the human devices and all machine stitching was completed using the same sewing machines and set ups. The bovine model had vessels that were slightly smaller than the clinical range. Thus the aortic diameter was reduced from 24mm to 22mm, the ipsilateral leg diameter was reduced from 12mm to 10mm and the contralateral leg reduced from 12mm to 11mm.

The study data evaluated acute technical success (deployment), stent graft integrity and the histopathological response to the Aorfix™ AAA Flexible Stent Graft System for up to 26 weeks. The results demonstrated the accurate deployment of the endovascular graft and the capacity of the prosthesis to maintain physiological function. The responses of both the host and prosthesis were acceptable and support the safety and expected performance of the Aorfix™ AAA Flexible Stent Graft System.

Table 5 Summary of Animal Studies

Study	Model	Samples	Details	Outcomes
Ovine	Adult female sheep 65kg to 75kg	12 tube devices implanted 2 sizes of tubular implant: 7cm x 14mm (majority) and 10cm x 12mm. Delivery system 18Fr outside diameter from standard sheath with modified core.	Phase 1a: 3 x Stand alone aneurysm model. 3 Months	Patent, unchanged at 3 months. Conclude model is viable.
			Phase 1b: 3 x implant into normal aorta. 6 Months	100% deployment succes, widely patent, free from migration at 6 months.
			Phase 2 a: 6 x implant placed to exclude preplaced aneurysm. 6 Months	100% deployment success but 2/9 early paraplegia secondary to access vessel thrombosis. Out of 7 stented aneurysms, 5 showed continuous shrinkage and became unrecognisable on 4-months scans. In two cases the size of aneurysm remained unchanged i.e. 6 cm and, Doppler studies suggested endoleak. On explantation the causes were revealed to be inadequate over-size (1) and inadequate length (1). Necropsy at 6 months showed stents were either partially or entirely covered by neointima. No migration was observed, with all hooks penetrating through aortic wall.
			Phase 2b: 3 x implant placed to exclude preplaced aneurysm from Phase 1a. 6 Months	

Study	Model	Samples	Details	Outcomes
Bovine	Young adult female calves aproxmately 200kg	8 Bifurcated endovascular stent grafts implanted in 8 animals	4 x acute animals < 1.5 hours	The device was sucessfully delivered to the target site within the infrarenal aorta with no related morbidity or mortality. The device delivery caused no vascular damage.
			4 x chronic animals followed for 100 to 115 days	The Aorfix™ AAA endoluminal stent graft system appears to be safe when implanted into the aortic bifurcation of young adult cattle. The healing response was normal. The histologic findings were comparable between animals and consistent with the implant of foreign material in the vascular system of a ruminant animal. All grafts were well incorporated into the intima of the native vessel and covered with a smooth neo-intima.

D. Sterilization, Packaging and Shelf-life

The Aorfix™ AAA Flexible Stent Graft System is a single-use device that is provided sterile to the end user. The Aorfix™ AAA Flexible Stent Graft System is sterilized using ETO sterilization and is validated to demonstrate a Sterility Assurance Level (SAL) of 10^{-6}**.** Packaging performance and stability testing demonstrate that the packaging designs for the Aorfix™ AAA Flexible Stent Graft System are sufficient to adequately protect the device and maintain the integrity of the Aorfix™ AAA Flexible Stent Graft System package throughout its 2-year shelf-life claim.

Shelf-life testing results are presented alongside the *in-vitro* bench test results as part of Table 4**.** Accelerated shelf-life product testing conducted on the Aorfix™ AAA Flexible Stent Graft System supports a 2-year shelf-life claim.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study (Pythagoras) to establish a reasonable assurance of safety and effectiveness of endovascular stent grafting with the Aorfix™ AAA Flexible Stent Graft System for infrarenal aortic and aorto-iliac aneurysms; however an adequate number of isolated iliac aneurysms were not enrolled in the study to demonstrate safety and effectiveness for this indication. The study anticipated enrolling a limited number of neck angles of <60° (for training purposes) and a majority of 60°-90° neck angles. The study was conducted under IDE #G050116 and was a controlled, prospective, non-randomized, multi-center study. Two hundred eighteen (218) Aorfix™ subjects and 76 Concurrent Open Surgical (COS) subjects were enrolled in this study.

The study was carried out at 41 hospitals in the US, 3 in Canada and 1 in Poland. Two hundred ten (210) Aorfix™ procedures were initiated in the US, 6 in Canada and 2 in

Poland. The most frequent number of procedures completed at each site was 2, illustrating low levels of experience with the Aorfix™ at many sites.

A. Study Design

The Pythagoras study was an open label, non-randomized study of Aorfix™. The Aorfix™ arm was compared with the COS control and with historical data from the Society for Vascular Surgery (SVS) Lifeline registry. The control group used open surgery because it is currently the only approved intervention for AAA subjects with aortic neck angles greater than 60° in the U.S.

Subjects were treated between April 28, 2006 and September 30, 2011. The database for this PMA reflected data collected through July 13, 2012 and included 218 Aorfix™ subjects and 76 COS subjects. An independent core lab reviewed CT scans and abdominal x-rays to assess all components of the primary efficacy endpoint including aneurysm changes, device integrity and position, and the presence of endoleaks. An independent Data Monitoring Committee (DMC) was established to ensure overall safety of the study and to classify secondary endpoints requiring clinical judgment.

The determination of the safety and effectiveness of the Aorfix™ AAA Flexible Stent Graft System was based on the data collected in the first year post-implant. Additionally, Lombard Medical has been following and will continue to follow the subjects enrolled in the Pythagoras study for a total of 5 years.

The Aorfix™ arm was divided into three sub-groups according to angle of the aortic neck. The first was based on the pre-specified hypotheses to be tested, including those subjects with neck angles from 60° to 90°. The other 2 were defined post-hoc, and included those subjects with neck angles less than 60° and those subjects with neck angles equal to or greater than 60°.

The objective of the Aorfix™ AAA Flexible Stent Graft System Pythagoras study was to evaluate the safety and effectiveness of the Aorfix™ AAA Flexible Stent Graft System in the treatment of aortic, iliac, and abdominal aorto-iliac aneurysms. As a result of low numbers of subjects (3) recruited with aneurysms only in their iliac vessels, the study did not have the power to support an indication for patients with iliac aneurysms who did not also have aortic aneurysms.

Effectiveness was assessed at 12 months in Aorfix™ AAA Flexible Stent Graft System subjects by a composite of those subjects free of Type I or Type III endoleak, free from migration > 10mm and free from fracture in the fixation zone.

Safety was assessed in Aorfix™ and COS subjects by evaluating the proportion of Aorfix™ subjects free from any Major Adverse Event (MAE) in the first 30 days postoperative and first 12 months postoperative compared with the control arm.

Pre-Specified Analysis

Although the study enrolled subjects with neck angles of less than 60° and greater than 90°, the study protocol's pre-specified analyses plan defined the primary analysis group as subjects with neck angles of 60° to 90°. For effectiveness, a sample size of 120 subjects was considered to be sufficient to achieve a minimum of 85% statistical power with a Type I error rate of 2.5%. The null hypothesis was that the proportion of subjects with aortic neck angles between 60° and 90° who were free of all components of the primary composite outcome at 12 months would be at least 80%.

The components of the effectiveness composite endpoints were:

- Type I and Type III endoleaks
- Migration of the proximal end of the device of more than 10mm
- Fracture in the fixation zone.

The primary safety hypothesis was that the proportion of subjects free from the occurrence of any Major Adverse Event (MAE) within 30 days of the implantation would be superior to the control group. The primary safety endpoint was defined as the rate of MAEs (as described below) within 30 days of the procedure. The sample size would provide 85% power to detect a rate difference of 0.14 for the 30-day Major Adverse Events between the two groups with an alpha of 0.05, using a two-sided two-sample chi-square test.

Changes to Pre-Specified Analysis

The study anticipated enrolling a limited number of neck angles of <60° (for training purposes) and a majority of subjects with neck angles of 60° to 90°. Subjects of >90° neck angles were inadvertently enrolled into the study due to variations in measuring techniques used at the clinical sites and the core laboratory. For purposes of analysis, the subjects were assigned to a neck angle group on the basis of the neck angle measured by the core lab. In this sense, the study was blinded to neck angle group but a consequence was that a substantial number of subjects were found to have higher neck angles than the study required.

The study ultimately enrolled 67 subjects with neck angles less than 60°, 109 with 60° to 90°, and 42 with >90°. Table 9 provides the distribution of neck angles of subjects enrolled in the study. After consultation with the FDA, it was decided that the post-hoc safety analysis would be conducted on the <60° population, the ≥60° population, and the <60° and ≥60° subjects combined (218). These three groups are presented below. When pertinent, the 60° to 90° results are also discussed to address the requirements of the pre-specified analysis. The effectiveness analysis presented below was conducted on the subjects who successfully received an Aorfix™ graft (210 subjects) who also had adequate data to evaluate the effectiveness endpoints.

All endpoints described in the pre-specified analysis plan were evaluated. Additional analysis requested by the FDA was also performed. Of specific note, due to missing data

the primary effectiveness endpoint employs a substitution assessment where later follow-up data is used to increase the robustness of the primary analysis.

The prospectively defined analysis also stipulated that the open control group would be the SVS Lifeline registry augmented by the COS control group. Due to limitations of the SVS registry including the lack of core lab defined neck angle measurements and the temporal differences in treatment between the Aorfix™ arm and the SVS registry, after consultation with the FDA it was decided that the COS arm would be the primary comparator for the study.

In addition, the prospective analysis allowed for expanded follow-up windows of: 30 days –7/+15 days; 6 months (defined as 180 days ± 1 month); 12 months (365 days ± 2 months); yearly to 5 years (365 days ± 2 months). In order to account for all visits, including those that occurred in between the visits noted above, expanded windows were defined and used in the analysis as noted in Table 6 and Table 7.

Finally, after consultation with the FDA, in addition to the substitution imputation discussed above, a tipping point analysis was performed to address missing data.

1. All Subjects Clinical Inclusion and Exclusion Criteria

Enrollment in the Aorfix™ AAA Flexible Stent Graft System Pythagoras Study was limited to subjects who met the following selection criteria as listed below:

- Diagnosed abdominal aortic aneurysm > 4.5 cm in diameter, OR 4.0 cm or larger in diameter if symptomatic (i.e. pain, embolisation), OR documented AAA growth of more than 5 mm within the previous 6 months, and/or including extension into common iliac artery(ies); and/or
- Iliac aneurysm greater than, or equal to 3.5 cm in maximum diameter.

Patients were not permitted to enroll in the Aorfix™ AAA Flexible Stent Graft System Pythagoras Study if they met any of the following exclusion criteria:

- Less than 21 years of age;
- Patient not expected to live more than 2 years from enrollment;
- Pregnant;
- Religious, cultural or other objection to the receipt of blood or blood products;
- Unwillingness to comply with follow-up schedule;
- Unwillingness or inability to provide informed consent to both trial and procedure;
- Patient had a ruptured aneurysm;
- Aneurysm extended above renal arteries;
- Aorta between superior mesenteric artery (SMA) and aneurysm had significant loose thrombus associated with it;

- Patient with an acute or chronic aortic dissection or mycotic aneurysm,
- Patient had current non-localized infection (may be recruited following remission of the infection);
- Patient was allergic to device materials;
- Patient was allergic to or intolerant of use of contrast media and could not be exposed to suitable remedial treatment such as steroids and/or Benadryl;
- Patient was clinically and morbidly obese such that imaging would be severely adversely affected;
- Patient had renal failure (serum creatinine > 2.5mg/dL);
- Patient had an uncorrectable bleeding abnormality;
- Patient had unstable angina;
- Patient was receiving dialysis;
- Inflammatory aneurysm;
- MI in prior 6 months;
- End stage COPD;
- Patient had connective tissue disease (e.g., Marfan syndrome, Ehlers Danlos syndrome); or
- Significant (>80%) renal artery stenosis which could not be readily treated.

Endovascular Arm Exclusion Criteria

- Patient had co-morbidities that deny vascular access, or small access vessels;
- Patient had highly calcified and/or tortuous proximal neck or distal landing zones or iliac arteries;
- Patient had insufficient length of proximal aneurysm neck (< 15mm from lowest renal artery) or SMA to aneurysm distance is less than 20mm;
- Patient had insufficient length of distal landing zone (< 15mm);
- Proximal neck was outside of device range indicated in IFU;
- The iliac artery diameter (landing zone) was larger than 19 mm in diameter (reference sizing tables);
- Indispensable Inferior Mesenteric Artery (IMA);
- Inability to maintain at least 1 patent hypogastric artery; or
- Excessive calcification, such as a ring or near ring of calcified plaque around an iliac artery.

Prospective participants excluded from the endovascular study arms could still be eligible for inclusion in the open arm. The acceptability of excessive tortuosity, calcification and thrombus was determined by the principal investigator at each site.

Open Arm Exclusion Criteria

- Excessive calcification or occlusive disease which would prevent open repair in the opinion of the principal site investigator;
- Any portion of the aneurysm was supra-renal;
- Aneurysm involved visceral arteries; or
- Otherwise eligible for the endovascular arm.

2. Follow-up Schedule

All subjects were scheduled to return for follow-up examinations at the following intervals postoperatively:

- 1 month following index procedure
- 6 months following index procedure
- 12 months following the index procedure; and
- Annually thereafter, for total of 5 years from the index procedure

At the 1 month and 12 month visits, abdominal X-ray and CT with contrast medium were required. Only an abdominal X-ray was required at the 6 months visit unless an endoleak was present at 30 days and then a CT was required. The alternative imaging modality, Duplex Ultrasound was recommended in subjects with impaired renal function or intolerance to contrast media. 'KUB' refers to a plane film abdominal X-ray covering the kidneys, ureters and bladder which was used to evaluate the device for possible fracture.

3. Clinical Endpoints

The analysis included clinically relevant endpoints for subjects with abdominal aortic disease. The endpoints used by Lombard Medical to demonstrate the safety of their device were adequate to describe the adverse events resulting from using the Aorfix™ AAA Flexible Stent Graft System. Similarly, endpoints used by Lombard Medical to demonstrate the effectiveness of their device were adequate to demonstrate the treatment effect.

With regards to safety, the primary safety post-hoc endpoint of the study evaluated all Aorfix™ subjects ($<60°$ and $\geq 60°$). The primary post-hoc safety endpoint compares the proportion of Aorfix™ subjects free from any MAE in the first 30 days postoperative with the rate in the COS arm.

The primary safety endpoint was further supported by a secondary safety analysis that was performed comparing Aorfix™ groups with results from the SVS Lifeline registry of open control subjects. This registry uses its own set of body system-related MAEs, referred to as SVS MAEs. The SVS MAE definition is less inclusive than the definition used by the study protocol for MAEs, principally because it defines no implant-specific events, such as 'Device replacement or revision.'

12 month secondary analyses included the proportion of Aorfix™ subjects free from: any MAE, all-cause mortality, aneurysm-related mortality, graft migration, graft fracture and endoleaks. In addition, changes in volume of aneurysms, changes in diameter of aneurysms, stent graft patency, conversions, aneurysm ruptures, secondary procedures, and procedural success were analyzed.

With regards to effectiveness, the primary effectiveness endpoint was the proportion of subjects in the Aorfix™ group classified as being free of all components of the primary composite endpoint at 12 months and was compared with 0.80. The components of the primary composite endpoint were migration > 10mm, fracture in the fixation zone and Type I or Type III endoleaks.

A core lab was used to standardize all measurements and assessments made from all images, including endoleak identification and classification and the determination of assessability of CTs. Core lab derived angle measurements were used to define the groups.

Post-hoc secondary outcomes included technical success at 30 days as adjudicated by an independent data monitoring committee (DMC).

B. Accountability of PMA Cohort

Follow-up evaluations were conducted at 1 month, 6 months (if needed), 12 months, and annually thereafter for a total of 5 years from the index procedure.

Although at 12 months, 86% of subjects had CT follow-up and 81% had KUB follow-up, detailed imaging deficits, such as lack of contrast enhancement or poor KUB image quality, substantially reduced the proportion of subjects with assessable data for the effectiveness endpoint.

At the time of database lock, 221 Aorfix™ subjects were consented in the PMA study. Of these, Aorfix™ implantation was not attempted in 2 subjects due to scheduling and graft availability and in 1 subject due to deteriorating health.

Therefore, 218 subjects had an Aorfix™ procedure initiated with the Intention To Treat (ITT Population). Of these, 8 subjects did not have an Aorfix™ graft successfully deployed, leaving 210 subjects that completed the Aorfix™ procedure (As Treated population). Subjects were unable to be followed-up for effectiveness purposes if they had not had an Aorfix™ graft implanted, had died or withdrawn from the study, had their Aorfix™ repair converted to an open repair, were lost to follow-up or were not yet due for follow-up.

Two hundred seven (207) subjects who received the stent graft were eligible for follow-up at 30 days. Of these, 189 (91%) had a clinical follow-up visit and 173 (84%) had CT scans. The 30 day follow-up window extended from 23 to 150 postoperative days.

One hundred forty-eight (148) subjects presented for a 6 month clinical visit. Although the protocol did not require a CT scan at the 6 month visit, 109 subjects had a CT performed.

At the 12 month follow-up interval, 196 subjects were eligible for clinical and imaging follow-up. Of these, 171 (87%) had clinical follow-up visits and 168 (86%) had CT scans performed. The 12 month follow-up window extended from 10 months to 22 months. Table 6 summarizes subject and scan accountability.

In the pre-specified analysis group of neck angles of 60° to 90°, 108 were eligible for 30 day follow-up, 99 subjects (92%) presented for a clinical follow-up and 91 (84%) had CT scans performed. One hundred and one (101) were eligible for a 12 month follow-up, 91 (90%) presented for a clinical follow-up and 87 (86%) had CT scans performed.

In the COS group, 76 were eligible for 30 day follow-up, 76 subjects (100%) presented for a clinical follow-up. Seventy one (71) were eligible for a 12 month follow-up, 62 (87%) presented for a clinical follow-up.

Data analysis sample sizes vary for each of the time points below and in the following tables. This variability is due to subject availability for follow-up as well as quality of images available from specific time points for evaluation. Although measures were undertaken to attempt 100% follow-up, this did not occur due to subject's health status, geographic proximity to evaluating physician, and core lab determined imaging quality.

Table 6 Subject Accountability and Follow-up, for Patients with an Aorfix™ Implanted

N (%) All Aorfix™ Subjects	Number of Subjects					Assessable Endpoints					Before Next Visit				
	Expected[1]	Clinical Evaluation	CT	KUB	Pending[2]	All Assessable[3]	Change in Aneurysm size4	Endoleak and Patency	Migration[4]	Fracture	Death	Withdrawal	Conversion	Lost to Follow-up	Not due for next visit
Subjects Implanted	**210**	**210 (100)**													
Reasons not eligible for next visit											**3**				
30 days expanded (23 to 150 days)	**207**	**189 (91.3)**	**173 (83.6)**	**166 (80.2)**		**138 (66.7)**		**163 (78.7)**		**160 (77.3)**					
Reasons not eligible for next visit											**2**	**1**	**1**		
6 months (5 to 7 months)	**203**	**148 (72.9)**	**109[5] (53.7)**	**139 (68.5)**		**81 (39.9)**		**101 (49.8)**		**136 (67)**					
Reasons not eligible for next visit											**4**				**3**
12 months expanded (10 to 22 months)	**196**	**171 (87.2)**	**168 (85.7)**	**158 (80.6)**	**6 (3.1)**	**124 (63.3)**	**168 (85.7)**	**143 (73)**	**160 (81.6)**	**150 (76.5)**					
Reasons not eligible for next visit											**14**	**4**		**3**	**23**
24 months expanded (22 to 34 months)	**152**	**134 (88.2)**	**127 (83.6)**	**116 (76.3)**	**8 (5.3)**	**79 (52)**	**127 (83.6)**	**102 (67.1)**	**119 (78.3)**	**103 (67.8)**					
Reasons not eligible for next visit											**9**	**2**		**1**	**28**
36 months expanded (34 to 46 months)	**112**	**85 (75.9)**	**80 (71.4)**	**76 (67.9)**	**17 (15.2)**	**55 (49.1)**	**79 (70.5)**	**69 (61.6)**	**75 (67)**	**67 (59.8)**					
Reasons not eligible for next visit											**7**	**2**		**2**	**51**
48 months expanded (46 to 58 months)	**50**	**21 (42)**	**19 (38)**	**16 (32)**	**25 (50)**	**12 (24)**	**19 (38)**	**16 (32)**	**19 (38)**	**14 (28)**					
Reasons not eligible for next visit											**2**	**1**		**1**	**37**
60 months expanded (>58 months)	**9**	**6 (66.7)**	**4 (44.4)**	**4 (44.4)**	**3 (33.3)**	**3 (33.3)**	**4 (44.4)**	**3 (33.3)**	**4 (44.4)**	**4 (44.4)**					

[1] N Expected is the number of subjects previously eligible for follow-up, minus those that have terminated or are not yet due for the visit.
[2] Subjects within visit window, but no data yet available.
[3] Subjects with data assessable for stent graft patency, endoleak, and stent fracture through 6 months plus change in aneurysm size and migration from 12 months onward.

[4] Subjects with scans 1-150 days postoperative and respective follow-up.
[5] Not required by protocol.

Table 7 Subject Accountability and Follow-up in the COS Arm

N (%) All COS Subjects	Subjects		Before next visit	
	Expected[1]	Clinical Evaluation	Death	Withdrawal
Subjects	76	76 (100)	0	0
Events after implant but before a 30 day visit	0	0	1	
30 days expanded (23 to 150 days)	75	69 (92)	0	0
Events after 30 day visit but before a 6 month visit	0	0	2	0
6 months (5 to 7 months)	73	42[2] (57.5)	0	0
Events after 6 month visit but before a 12 month visit	0	0	1	1
12 months expanded (10-22 months)	71	62 (87.3)		

[1] N Expected is the number of subjects previously eligible for follow-up, minus those that have terminated or are not yet due for the visit.
[2] Not required by protocol.

C. Study Population Demographics and Baseline Parameters

The demographic data for the Aorfix™ ITT population and the COS ITT population are presented and compared in Table 8 while the medical histories of the two populations are presented in Table 9. On average the Aorfix™ ITT subjects represent a significantly older subject population (76 vs. 69; $p<0.001$). The proportion of female subjects treated was substantially higher in the Aorfix™ ITT population compared with the COS ITT population (29% vs. 20%). This difference is particularly influenced by the Aorfix™ ITT ≥60° group in which 35% of subjects were female, which was significantly more than the COS ITT population ($p=0.017$).

A significantly higher proportion of the COS ITT population presented with history of tobacco use (97% vs. 87%; $p=0.008$). There were also several notable differences in baseline medical history between the Aorfix™ ITT population and the COS ITT population which failed to reach significance because of limited subject numbers. Comparing Aorfix™ ITT with COS ITT, Congestive heart failure (13% vs. 5.4%), Angina (11% vs. 5.3%), Liver disease (4.6% vs. 1.3%) and Renal disease (14.3% vs. 6.7%) have more than double the incidence in the Aorfix™ ITT population than in the COS ITT. Coagulopathy (1.4% vs. 5.3%), alcohol abuse (3.2% vs. 8%) and peripheral

artery occlusive disease (10% vs. 17%) had lower incidence in the Aorfix™ ITT population than in the COS ITT.

The data presented below is grouped in the post-hoc analysis groups. The pre-defined group of 60° to 90° showed a similar mean age of 76 years and similar percent females at 28%. The baseline medical histories of the 60° to 90° group were similar to those of the ≥60° group.

Table 8 Demographics

N Mean ±STD % (n/N)	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Mean Age				
Age	n=67 74.0▲ ±7.92	n=151 76.3▲ ±7.24	n=218 75.6▲ ±7.51	n=76 69.2 ±7.04
Age Category▲▲				
≤55 years	1.5% (1/67)	0	0.5% (1/218)	3.9% (3/76)
56-65 years	16.4% (11/67)	9.3% (14/151)	11.5% (25/218)	26.3% (20/76)
66-75 years	34.3% (23/67)	35.8% (54/151)	35.3% (77/218)	48.7% (37/76)
76-85 years	43.3% (29/67)	47.7% (72/151)	46.3% (101/218)	21.1% (16/76)
≥86 years	4.5% (3/67)	7.3% (11/151)	6.4% (14/218)	0
Gender				
Male	85.1% (57/67)	64.9%▲ (98/151)	71.1% (155/218)	80.3% (61/76)
Female	14.9% (10/67)	35.1%▲ (52/151)	28.9% (63/218)	19.7% (15/76)
Ethnicity				
White, non-Hispanic	94.0% (63/67)	91.4% (138/151)	92.2% (201/218)	90.8% (69/76)
Non-White	6.0 % (4/67)	8.6% (13/151)	7.8% (17/218)	9.2% (7/76)

▲indicates difference between each Aorfix™ ITT group and the COS ITT population p≤0.05
▲▲ The distribution of ages is significantly different from COS ITT for all Aorfix™ ITT subgroups

Table 9 Baseline Medical History

% (n/N▲▲) Body System/Condition	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Patients with at Least One Condition	100.0% (67/67)	99.3% (150/151)	99.5% (217/218)	100.0% (76/76)
Cardiovascular	94.0% (63/67)	94.0% (142/151)	94.0% (205/218)	88.2% (67/76)
Angina	9.0% (6/67)	11.9% (18/151)	11.0% (24/218)	5.3% (4/67)
Arrhythmia	16.4% (11/67)	23.8% (36/151)	21.6% (47/218)	21.1% (16/76)
Coagulopathy	4.5% (3/67)	0▲	1.4% (3/215)	5.3% (4/76)
Congestive Heart Failure	10.8% (7/65)	13.4% (20/149)	12.6% (7/214)	5.4% (4/74)
Coronary Artery Disease	50.7% (34/67)	43.6% (65/149)	45.8% (99/216)	37.0% (27/73)
History of Stroke or TIA	15.4% (10/65)	12.6% (19/ 151)	13.4% (29/216)	7.9% (6/76)
Hypertension	89.6% (60/67)	83.3% (125/150)	85.3% (185/217)	80.3% (61/76)
Myocardial Infarction	32.8% (22/67)	20.8% (31/149)	24.5% (53/216)	25.0% (19/76
Peripheral Arterial Occlusive Disease	10.8% (7/65)	9.9% (14/142)	10.1% (21/207)	17.1% (12/70)
Valvular Disease	9.0% (6/67)	11.3% (17/151)	10.6% (23/218)	7.9% (6/76)
Other	98.5% (66/67)	98.0% (148/ 151)	98.2% (214/218)	98.7% (75/76)
Alcohol Abuse	6.0% (4/67)	2.0% (3/150)	3.2% (7/217)	8.0% (6/75)
Allergy to Contrast	6.0% (4/67)	3.3% (5/151)	4.1% (9/218)	2.6% (2/76)
Allergy to Nickel	0	0	0	0
Allergy to Penicillin	9.0% (6/67)	11.9% (18/151)	11.0% (24/218)	9.2% (7/76)
Cancer	27.3% (18/66)	30.5% (46/151)	29.5% (64/217)	23.7% (18/76)
Diabetes	19.4% (13/67)	16.7% (25/150)	17.5% (38/217)	12.0% (9/75)
Family History of AAA Disease	27.6% (16/58)	20.1% (27/134)	22.4% (43/192)	25.4% (17/67)
Liver Disease	7.5% (5/67)	3.3% (5/151)	4.6% (10/218)	1.3% (1/75)
Obesity	19.4% (13/67)	13.9% (21/151)	15.6% (34/218)	21.1% (16/76)
Other Chronic Disease	15.4% (10/65)	30.7% (46/150)	26.0% (56/215)	22.7% (17/75)
Pulmonary Insufficiency	28.4% (19/67)	33.3% (49/147)	31.8% (68/214)	28.2% (20/71)
Seasonal/Other Allergies	25.4% (17/67)	29.8% (45/151)	28.4% (62/218)	17.1% (13/76)
Tobacco Use	97.0% (65/67)	82.8%▲ (125/151)	87.2%▲ (190/218)	97.4% (74/76)
Wound Infection	0	0.7% (1/151)	0.5% (1/218)	0
Renal Disease	13.4% (9/67)	14.7% (22/150)	14.3% (31/217)	6.7% (5/75)

▲indicates difference between each Aorfix™ ITT group and the COS ITT population $p \leq 0.05$

▲▲Sample sizes vary for specific baseline medical conditions due to missing data at the time of report writing.

Average neck length in the COS ITT was shorter than in the Aorfix™ ITT population while average neck angles were higher in the Aorfix™ ITT population than in the COS ITT population. These measurements apart, the preoperative CT measurements showed all other dimensions, including the range and distribution of aneurysm diameters, to be generally comparable across the control population and the Aorfix™ population. Table 10 to Table 12 summarize aneurysm and access vessel characteristics.

Table 10 Baseline Aneurysm and Access Vessel Characteristics

N Mean ± SD	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Iliac Aneurysm without AAA	0	2.0% (3/151)	1.4% (3/218)	0
Iliac Aneurysm with AAA	3.0% (2/67)	2.0% (3/151)	2.3% (5/218)	6.6% (5/76)
Proximal Neck Diameter 1mm Infrarenal (mm)	n=67 23.41 ± 3.41	n=151 22.23▲ ± 2.72	n=218 22.59▲ ± 2.99	n=75 24.82 ± 5.17
Proximal Neck Diameter 7mm Infrarenal (mm)	n=67 23.25▲ ± 3.12	n=151 22.44▲ ± 3.15	n=218 22.69▲ ± 3.16	n=75 27.90 ± 6.79
Proximal Neck Diameter 15mm Infrarenal (mm)	n=67 25.08▲ ± 4.30	n=151 24.14▲ ± 5.64	n=218 24.43▲ ± 5.27	n=75 32.90 ± 8.77
Proximal Neck Length (mm)	n=67 24.04▲ ± 15.38	n=151 21.91▲ ± 12.60	n=218 22.56▲ ± 13.51	n=75 13.34 ± 12.74
Proximal Neck Angle (°)	n=67 44.75 ± 12.32	n=151 83.26▲ ± 14.51	n=218 71.42▲ ± 22.56	n=75 48.24 ± 23.26
Sac Diameter (mm)	n=67 54.31▲ ± 8.98	n=151 58.95 ± 11.93	n=218 57.53 ± 11.29	n=75 57.69 ± 8.76
Sac Volume (cc)	n=66 168.01▲ ± 68.36	n=151 218.37 ± 108.21	n=217 203.05 ± 100.38	n=74 200.82 ± 88.68
Maximum Left Iliac Diameter (mm)	n=66 17.28 ± 4.50	n=151 19.73▲ ± 9.50	n=217 18.99 ± 8.37	n=72 17.27 ± 6.38
Maximum Right Iliac Diameter (mm)	n=66 17.53 ± 4.60	n=151 21.02▲ ± 9.06	n=217 19.96 ± 8.12	n=74 18.54 ± 7.69
Proximal Neck Diameter (mm)	n=67 25.79▲ ± 3.18	n=151 24.27▲ ± 3.02	n=218 24.74▲ ± 3.14	n=75 27.49 ± 5.48

▲indicates difference between each Aorfix™ ITT group and the COS ITT population $p \leq 0.05$

Table 11 Distribution of Aneurysm Diameters

% (n/N) Max. Aneurysm Diameter (mm)	Aorfix™ <60° N`=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
<30	0	0.7% (1/151)	0.5% (1/218)	0
30 to <40	0	1.3% (2/151)	0.9% (2/218)	1.3% (1/76)
40 to <50	38.8% (26/67)	14.6% (22/151)	22% (48/218)	14.7% (11/76)
50 to <60	40.3% (27/67)	47.0% (71/151)	45.0% (98/218)	46.7% (35/76)
60 to <70	14.9% (10/67)	20.5% (31/151)	18.8% (41/218)	25.3% (19/76)
70 to <80	4.5% (3/67)	10.6% (16/151)	8.7% (19/218)	10.7% (8/76)
80 to <90	1.5% (1/67)	3.3% (5/151)	2.8% (6/218)	1.3% (1/76)
≥90	0	2.0% (3/151)	1.4% (3/218)	0

Table 12 Distribution of Aortic Neck Angles

% (n/N) Aneurysm Neck Angles (°)	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
<40°	26.9% (18/67)		8.3% (18/218)	37.3% (28/76)
40° to <50°	26.9% (18/67)		8.3% (18/218)	18.7% (14/76)
50° to <60°	46.3% (31/67)		14.2% (31/218)	17.3% (13/76)
60° to <70°		15.9% (24/151)	11.0% (24/218)	10.7% (8/76)
70° to <80°		29.1% (44/151)	20.2% (44/218)	9.3% (7/76)
80° to <90°		23.8% (36/151)	16.5% (36/218)	1.3% (1/76)
90° to <100°		22.5% (34/151)	15.6% (34/218)	2.7% (2/76)
≥100°		8.6% (13/151)	6.0% (13/218)	2.7% (2/76)

Tortuosity index is used to provide a ratio of the tortuosity of a vessel. It represents the extra length of a vessel between its origin and terminus, caused by tortuosity, compared with the length it would have had if it took a straight path.

Aorto-iliac tortuosity is calculated from the distal renal artery to the right or left femoral artery bifurcation and Iliac tortuosity is calculated from the aortic bifurcation to the right or left femoral artery bifurcation. For each group there is a substantial range of tortuosities. Tortuosity indices in the all angle Aorfix™ group are larger than the COS ITT group.

Table 13 Tortuosity Indices

N Mean ± SD	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Right Aorto-Iliac Tortuosity Index	n=66 1.239▲ ± 0.077	n=149 1.330▲ ± 0.101	n=215 1.302▲ ± 0.103	n=73 1.243 ± 0.107
Left Aorto-Iliac Tortuosity Index	n=66 1.251▲ ± 0.081	n=149 1.333▲ ± 0.114	n=215 1.308▲ ± 0.111	n=72 1.244 ± 0.105
Right Iliac Tortuosity Index	n=65 1.291 ± 0.121	n=149 1.325 ± 0.143	n=214 1.315 ± 0.137	Not Calculated
Left Iliac Tortuosity Index	n=65 1.272 ± 0.105	n=149 1.322 ± 0.154	n=214 1.307 ± 0.143	Not Calculated

▲indicates difference between each Aorfix™ ITT group and the COS ITT population p≤0.05

D. Devices Implanted

The Aorfix™ device is a two piece device comprising an aortic body with conjoined ipsilateral leg and a modular contralateral leg. Proximal extenders, distal extenders and an AUI converter can be used with the basic implants. Table 14 provides details of the number of Aorfix™ devices implanted per index procedure, Table 15 lists the number of devices implanted by Type and by neck angle, and Table 16 lists the number of devices implanted by diameter.

Table 14 Number of Devices Implanted

% (n/N) Number of Devices Implanted per Subject	Aorfix™ <60° As Treated N=67	Aorfix™ ≥60° As Treated N=143	Aorfix™ As Treated N=210
2	52.2% (35/67)	55.2% (79/143)	54.3% (114/210)
3	37.3% (25/67)	35.7% (51/143)	36.2% (76/210)
4	10.4% (7/67)[1]	9.1% (13/143)	9.0% (19/210)

[1]Includes 1 subject who at the time of lock, the database showed only one device used but operative report indicated 4 had been used.

Table 15 Devices Implanted by Type at Index Procedure

% (n/N) Device Type	Aorfix™ <60° As Treated N=67	Aorfix™ ≥60° As Treated N=143	Aorfix™ As Treated N=210
Bifurcated Body	100% (67/67)	100% (143/143)	100% (210/210)
Contralateral Leg	97.0% (65/67)	97.2% (139/143)	97.1% (204/210)
Distal Extender	47.8% (32/67)	36.4% (52/143)	40.0% (84/210)
Proximal Extender	7.5% (5/67)	18.2% (26/143)	14.8% (31/210)
Converter	1.5% (1/67)	2.1% (3/143)	1.9% (4/210)

Table 16 lists the numbers and sizes of devices recorded as used, taken from the ITT population. While full records are available on the types of devices implanted, in a minority of cases, accurate data on the size of implanted device was not available at the time of data-base lock. The denominators in the table reflect the numbers of each type of device (e.g., contralateral leg) or sizes of main body devices (i.e., body and ipsilateral leg) with complete data.

Table 16 Diameters of Devices Implanted

Aorfix™ Piece	Diameter (mm)	Aorfix™ ITT % (n/N)	
Body	24	26.6%	54/203
	25	3.0%	6/203
	26	17.2%	35/203
	27	5.9%	12/203
	28	23.6%	48/203
	29	3.9%	8/203
	30	3.9%	8/203
	31	15.8%	32/203
Ipsilateral Leg	10	0.5%	1/202
	12	19.3%	39/202
	14	13.9%	28/202
	16	35.1%	71/202
	18	8.9%	18/202
	20	22.3%	45/202
Contralateral Leg	10	2.6%	5/194
	12	18.0%	35/194
	14	19.1%	37/194
	16	24.2%	47/194
	18	13.4%	26/194
	20	22.7%	44/194
Distal Extender	10	1.3%	1/80
	12	22.5%	18/80
	14	21.3%	17/80
	16	22.5%	18/80
	18	6.3%	5/80
	20	26.3%	21/80
Proximal Extender	24	16.7%	5/30
	25	6.7%	2/30
	26	23.3%	7/30
	27	0	0
	28	26.7%	8/30
	29	6.7%	2/30
	30	0	0
	31	20.0%	6/30
Converter	25	60.0%	3/5
	27	20.0%	1/5
	29	20.0%	1/5
	31	0	0

E. Safety and Effectiveness Results

1. Acute Procedural Data and Technical Success:

1.1 Acute procedural outcomes: Procedure duration, blood loss, blood transfusion, fluoroscopy exposure time and length of stay in the hospital are presented in Table 17.

Table 17 Clinical Utility

n Mean ± STD % (n/N)	Aorfix™ <60° As Treated N=67	Aorfix™ ≥60° As Treated N=143	Aorfix™ As Treated N=210	COS As Treated N=76
Duration of procedure (min)	n=66 164.3 ±73.46	n=141 177.4 ±68.85	n=207 173.2 ±70.44	n=76 222.8 ±94.31
Hospital Stay (days)	n=66 3.3 ±1.92	n=143 4.1 ±3.87	n=209 3.9 ±3.39	n=76 8.9 ±4.28
Estimated blood loss	n=67 402.8 ±456.06	n=139 430.1 ±387.79	n=206 421.2 ±410.32	n=70 1377.1 ±1398.83
Fluoroscopy time (min)	n=65 29.5 ±17.69	n=141 37.4 ±24.45	n=206 34.9 ±22.79	0
Contrast Used (cc)	n=63 146.2 ±59.21	n=140 143.3 ±71.49	n=203 144.2 ±67.78	0
Subjects requiring transfusion	10.4% (7/67)	20.3% (29/143)	17.1% (36/210)	43.4% (33/76)
Percutaneous Access	19.4% (13/67)	17.5% (25/143)	18.1% (38/210)	0
Subjects receiving general anesthesia	82.1% (55/67)	83.8% (119/143)	83.3% (174/210)	98.7% (75/76)

1.2 Technical Success (Adjudicated by DMC): The DMC used a robust definition of technical success to ensure that the adjudications were a reliable indicator of true success. Technical success was assessed at 30 days post-operative and required successful access and deployment, freedom from Type I and III endoleak and freedom from additional intra-operative and post-operative procedures. Results are presented in terms of technical failure and are listed in Table 18 and Table 19.

Table 18 Technical and Procedural Failure (assessed in ITT Population)

% (n/N) Failure	Aorfix™ <60° As Treated N=61	Aorfix™ ≥60° As Treated N=146	Aorfix™ All As Treated N=207
Technical Failure (Intra-operative)	9.8% (6/61)	13.7% (20/146)	12.6% (26/207)
Technical Failure (Post-operative)	3.3% (2/61)	8.9% (13/146)	7.2% (15/207)
Technical Failure (All)	13.1% (8/61)	22.6% (33/146)	19.8% (41/207)

Data analysis sample sizes vary due to data available to DMC at time of report writing.

Table 19 Causes of Technical Failure

	Index	2ndy	Total (Index and 2ndy Procedures)	Explicitly Related MAE
Access Failure	2		**2**	2
Access Vessel Repair	3	4	**7**	1
Competitor Graft Used	3		**3**	0
Contained Rupture	1		**1**	1
Intra-Operative Conversion	3		**3**	2
Death within 30d	1	1	**2**	0
Delivery System Retrieval Difficulty	2		**2**	1
Hypercoaguable State		1	**1**	1
Leg Occlusion		5	**5**	4
Delivery System Failure in Highly Tortuous Access Vessels	1		**1**	1
Renal Event	6	2	**8**	0
SMA Stent Placement	1		**1**	1
Type Ia Endoleak	1	1	**2**	1
Type Ib Endoleak		1	**1**	1
Unplanned AUI Converter	1		**1**	1
Unplanned Distal Extender	1		**1**	0
Total	**26**	**15**	**41**	**17**

1.3 Technical Observations: Two (2) cases were identified with fractures of the wire form in the aortic part of the stent graft, just proximal to the flow divider. There were no clinical sequelae to the observations and in both cases significant sac volume reduction was seen.

In one subject, a delivery system tip detached while extending a limb into a narrow external iliac artery. Since that event, manufacturing processes have been modified to strengthen the attachment of the tip and the shape of the tip has been adjusted to reduce the risk of entrapment.

2. Safety Results

2.1 Major Adverse Events: Table 20 and Table 21 provide an analysis of the major adverse events within 30 days for the Aorfix™ ITT group. The data below, containing post-hoc analysis groups provides a comparison of the Aorfix™ ITT and the COS ITT freedom from MAEs within 30 days (76% versus 59%). Subjects in the Aorfix™ 60° to 90° pre-specified analysis group had 75% freedom from Major Adverse Events compared with 59% of subjects in the COS ITT control population. All subjects were evaluable within 30 days of the procedure.

Table 20 Major Adverse Events Free Rates (within 30 Days)

% (n/N) [95% CI]	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Freedom from any MAE within 30 days	82.1% (55/67) [72.9%- 91.3%]	72.8% (110/151) [65.8%- 79.9%]	75.7% (165/218) [70.0%- 81.4%]	59.2% (45/76) [48.2%-70.3%]

As anticipated, blood loss was the major event significantly improved by the use of Aorfix™. While not reaching statistical significance, Aorfix™ subjects had a higher rate of Congestive Heart Failure (CHF) events, possibly related to the higher baseline rates of CHF in that population. Compared with control, increased levels of graft thrombosis (3) and device revision (4) were seen in the Aorfix™ population.

Table 21 Major Adverse Event Components (within 30 Days)

% (n/N) MAE	Aorfix™ <60° N=67	Aorfix™ >=60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Excessive Bleeding Requiring Transfusion	9.0% (6/67)	13.9% (21/151)	12.4% (27/218)	35.5% (27/76)
Cardiac Arrest	0	0.7% (1/151)	0.5% (1/218)	0
Myocardial Infarction	1.5% (1/67)	2.0% (3/151)	1.8% (4/218)	0
Congestive Heart Failure	1.5% (1/67)	4.0% (6/151)	3.2% (7/218)	0
Pulmonary Failure	0	2.0% (3/151)	1.4% (3/218)	1.3% (1/76)
Renal Failure	0	1.3% (2/151)	0.9% (2/218)	1.3% (1/76)
Bowel Ischemia	0	0.7% (1/151)	0.5% (1/218)	0
Sepsis	0	0.7% (1/151)	0.5% (1/218)	0
Surgical Wound Complication	3.0% (2/67)	4.6% (7/151)	4.1% (9/218)	5.3% (4/76)

% (n/N) MAE	Aorfix™ <60° N=67	Aorfix™ >=60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Aneurysm Rupture	0	0	0	0
Graft Occlusion	1.5% (1/67)	2.0% (3/151)	1.8% (4/218)	1.3% (1/76)
Graft Thrombosis	0	2.0% (3/151)	1.4% (3/218)	0
Graft Infection	0	0	0	0
False Aneurysm	0	0	0	0
Device replacement or revision	1.5% (1/67)	2.0% (3/151)	1.8% (4/218)	0

Table 22 provides rates of major adverse events within 12 months. Sixty-seven percent (67%) of subjects in the Aorfix™ population were free from Major Adverse Events and 53.9% of subjects in the COS ITT control population.

Table 22 Rates of Freedom from Major Adverse Events (within 12 months)

% (n/N)	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT N=76
Freedom from any MAE within 12 months	74.6% (50/67)	64.2% (97/151)	67.4% (147/218)	53.9% (41/76)

2.2 Mortality: Table 23 provides the all-cause mortality free rate at 30 days and 12 months for the Aorfix™ ITT population and the COS ITT control population. The data below accounts for all deaths at 30 days and 365 days regardless of follow-up windows. See Table 6 for an accounting of deaths per time interval and follow-up window.

Table 23 All Cause Mortality-Free rate at 30 Days and 12 months

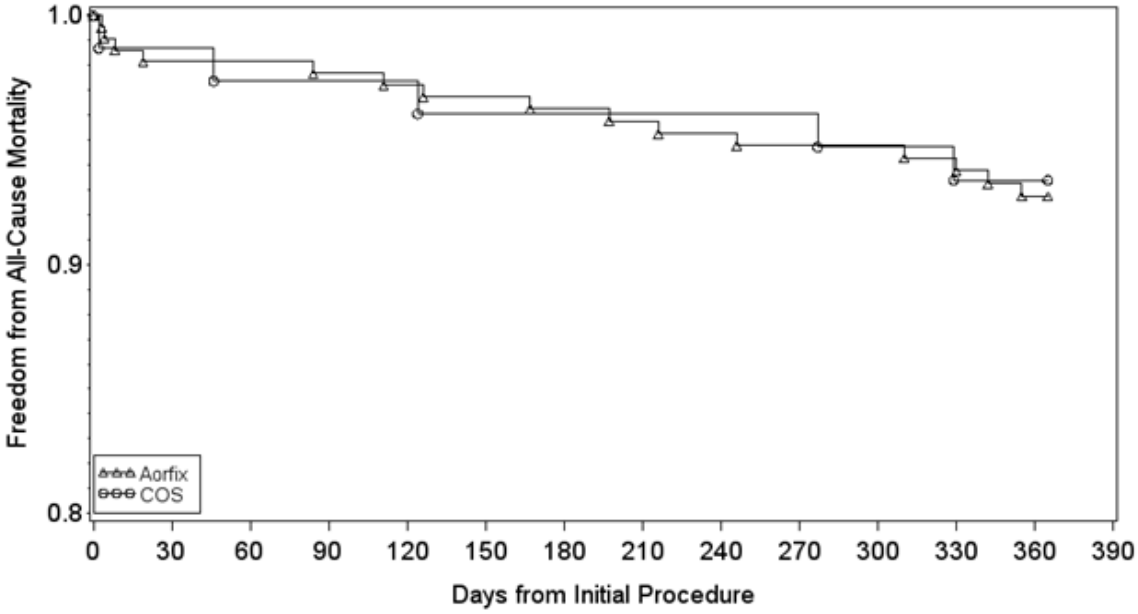
% (n/N)	Aorfix™ <60° (N=67)	Aorfix™ >=60° (N=151)	Aorfix™ ITT (N=218)	COS ITT (N=76)
All-Cause Mortality-Free Rate 30 Days	98.5% (66/67)	98.0% (148/151)	98.2% (214/218)	98.7% (75/76)
All-Cause Mortality-Free Rate at 12 months	95.5% (64/67)	92.1% (139/151)	93.1% (203/218)	93.4% (71/76)

Table 24 Lists the Kaplan-Meier estimates of All-Cause Mortality Free Rates for the Aorfix™ ITT and COS ITT populations and the estimates are plotted in Figure 13.

Table 24 Kaplan Meier estimate of rates of freedom from All-Cause Mortality at 12 months

% (Events/At Risk)	Treatment to 30 Days	31 Days to 182 Days	183 Days to 365 Days
All Aorfix™ ITT Subjects N	1.8% (4/218)	1.9% (4/211)	3.5% (7/200)
KM Estimate ± SE	0.981 ± 0.009	0.962 ± 0.013	0.927 ± 0.018
All COS ITT Subjects N	1.3% (1/76)	2.7% (2/75)	2.7% (2/73)
KM Estimate ± SE	0.987 ± 0.013	0.961 ± 0.022	0.934 ± 0.029

Figure 13 Kaplan-Meier Estimate of 1-Year Freedom from All-Cause Mortality



Aneurysm-related mortality was assessed by the DMC. All subjects dying prior to hospital discharge or within the first 30 post-operative days were included, to which were added those subjects who died directly from the aneurysm or as a consequence of revision surgery performed on the stent graft.

Aneurysm-related mortality free rate within 12 months was 98% and is shown in Table 25.

Table 25 Aneurysm-Related Mortality Free Rates at 30 days and 12 months

% (n/N)	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	COS ITT (N=76)
Aneurysm-Related Mortality Free, 30 days	98.4% (60/61)	97.9% (143/146)	98.1% (203/207)	98.7% (75/76)
Aneurysm-Related Mortality Free, 12 months	98.4% (60/61)	96.6% (141/146)	97.1% (201/207)	97.4% (74/76)

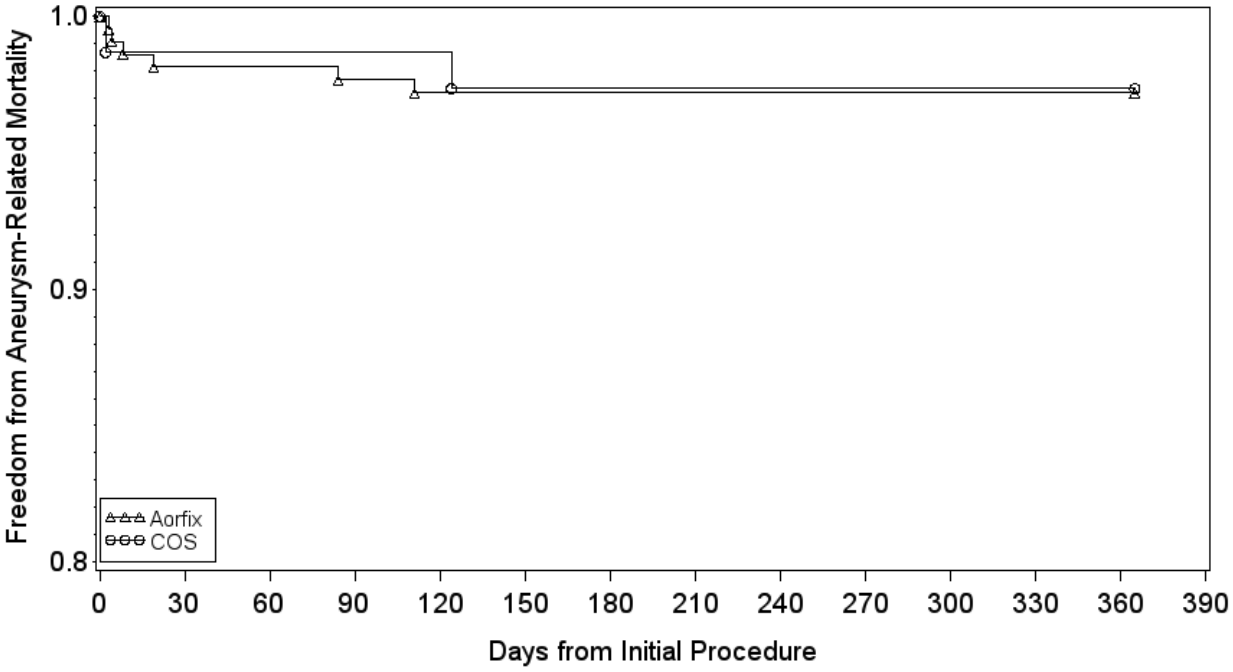
Data analysis sample represents data available to the DMC at time of review.

Table 26 lists the Kaplan Meier estimates for AAA-related mortality. Note that it is based on actual dates of death whereas in the MAE data, a death occurring pre-hospital discharge is counted as a 30-day death even if the discharge occurred after that date.

Table 26 Kaplan Meier Estimate of Aneurysm Related Mortality Free Rates at 12 months

% (Events/At Risk)	Treatment to 30 Days	31 Days to 182 Days	183 Days to 365 Days
All Aorfix™ ITT Subjects N	1.8% (4/218)	0.9% (2/211)	0% (0/200)
KM Estimate ± SE	0.981 ± 0.009	0.972 ± 0.011	0.972 ± 0.011
All COS ITT Subjects N	1.3% (1/76)	1.3% (1/75)	0% (0/73)
KM Estimate ± SE	0.987 ± 0.013	0.974 ± 0.018	0.974 ± 0.018

Figure 14 Kaplan Meier Estimate of Freedom from Aneurysm Related Mortality at 12 months



2.3 Adverse Events: Adverse events (AEs) for all enrolled subjects were categorized, and the total number of subjects with one or more AEs in each category and their relative percentages are summarized below for serious adverse events (SAEs), all AEs excluding SAEs, device- and procedure-related MAEs, device- and procedure-related SAEs and device- and procedure-related AEs.

Serious Adverse Events

A Serious Adverse Event (SAE) is one which, in the view of either the investigator or sponsor, results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention.

SAEs at 12 months as reported by the Aorfix™ AAA Flexible Stent Graft System clinical investigational sites are described in Table 27. As anticipated, over 12 months the COS subjects had higher rates of bleeding events compared with Aorfix™ (26.3% v 16.1%). In addition, 12 month gastrointestinal (14.5% vs. 3.7%) events are higher in COS group as are pulmonary / upper respiratory events at 30 days. The rate of events in the Aorfix™ groups were higher for cancer (3.2% vs. 1.3%), neurologic (5.5% vs. 1.3%), vascular (17.0% vs. 6.6%) and 'other' (6.0% vs. 2.6%). The larger rate of cancer events is most likely the result of patient selection, although the medical history of cancer was equivalent in both groups.

Table 27 Serious Adverse Events through 12 Months

% (n/N) SAE Category	0 to 30 Days		31 to 365 Days		0 to 365 Days	
	Aorfix™ ITT	COS ITT	Aorfix™ ITT	COS ITT	Aorfix™ ITT	COS ITT
	N=218	N=76	N=211	N=75	N=218	N=76
Any SAEs	33.9% (74/218)	38.2% (29/76)	27.5% (58/211)	21.3% (16/75)	47.2% (103/218)	50.0% (38/76)
Bleeding	15.1% (33/218)	25.0% (19/76)	2.4% (5/211)	1.3% (1/75)	16.1% (35/218)	26.3% (20/76)
Cancer	0.9% (2/218)	0	2.4% (5/211)	1.3% (1/75)	3.2% (7/218)	1.3% (1/76)
Cardiac	7.8% (17/218)	7.9% (6/76)	6.2% (13/211)	6.7% (5/75)	11.5% (25/218)	14.5% (11/76)
Gastrointestinal	2.3% (5/218)	7.9% (6/76)	1.4% (3/211)	6.7% (5/75)	3.7% (8/218)	14.5% (11/76)
Genitourinary	0.9% (2/218)	0	0.5% (1/211)	0	0.9% (2/218)	0
Infection	0.5% (1/218)	1.3% (1/76)	0.9% (2/211)	0	1.4% (3/218)	1.3% (1/76)
Neurologic	2.3% (5/218)	0	3.3% (7/211)	1.3% (1/75)	5.5% (12/218)	1.3% (1/76)
Orthopedic	0.9% (2/218)	1.3% (1/76)	2.8% (6/211)	0	3.2% (7/218)	1.3% (1/76)
Other	2.8% (6/218)	1.3% (1/76)	3.3% (7/211)	1.3% (1/75)	6.0% (13/218)	2.6% (2/76)
Pulmonary/Upper Respiratory	4.1% (9/218)	9.2% (7/76)	5.7% (12/211)	4.0% (3/75)	9.6% (21/218)	11.8% (9/76)
Renal	6.9% (15/218)	9.2% (7/76)	2.4% (5/211)	2.7% (2/75)	9.2% (20/218)	11.8% (9/76)
Unknown	0	0	0	1.3% (1/75)	0	1.3% (1/76)
Vascular	10.6% (23/218)	5.3% (4/76)	9.0% (19/211)	1.3% (1/75)	17.0% (37/218)	6.6% (5/76)
Wound	2.8% (6/218)	2.6% (2/76)	0.5% (1/211)	1.3% (1/75)	3.2% (7/218)	2.6% (2/76)

Adverse Events Excluding Serious Adverse Events (nSAEs)

Table 28 describes the Adverse Events (excluding SAEs) reported by the Aorfix™ AAA Flexible Stent Graft System clinical investigational sites. Table 33 lists the subset of non-serious AEs adjudicated by investigational sites to be device-related. Table 34 lists the subset of non-serious AEs adjudicated by investigational sites to be procedure-related. In a minority of cases, sites did not adjudicate whether an event was device- or procedure-related.

Table 28 Adverse Events Excluding SAEs through 12 Months

% (n/N) AE Category	0 to 30 Days		31 to 365 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=211	COS ITT N=75	Aorfix™ ITT N=218	COS ITT N=76
AEs (excl SAE)	62.4% (136/218)	78.9% (60/76)	36.5% (77/211)	41.3% (31/75)	73.4% (160/218)	85.5% (65/76)
Bleeding	24.3% (53/218)	26.3% (20/76)	3.3% (7/211)	1.3% (1/75)	25.7% (56/218)	27.6% (21/76)
Cancer	0.5% (1/218)	0	2.4% (5/211)	1.3% (1/75)	2.3% (5/218)	1.3% (1/76)
Cardiac	24.8% (54/218)	34.2% (26/76)	4.3% (9/211)	2.7% (2/75)	26.1% (57/218)	35.5% (27/76)
Edema	6.4% (14/218)	6.6% (5/76)	0.9% (2/211)	1.3% (1/75)	7.3% (16/218)	7.9% (6/76)
Gastrointestinal	22.9% (50/218)	34.2% (26/76)	3.8% (8/211)	14.7% (11/75)	24.8% (54/218)	42.1% (32/76)
Genitourinary	15.6% (34/218)	5.3% (4/76)	5.2% (11/211)	5.3% (4/75)	18.8% (41/218)	10.5% (8/76)
Infection	7.3% (16/218)	10.5% (8/76)	1.4% (3/211)	2.7% (2/75)	7.8% (17/218)	11.8% (9/76)
Neurologic	10.6% (23/218)	18.4% (14/76)	5.7% (12/211)	5.3% (4/75)	15.6% (34/218)	21.1% (16/76)
Orthopedic	11.0% (24/218)	1.3% (1/76)	4.7% (10/211)	8.0% (6/75)	14.7% (32/218)	9.2% (7/76)
Other	31.2% (68/218)	43.4% (33/76)	11.8% (25/211)	6.7% (5/75)	37.2% (81/218)	46.1% (35/76)
Pulmonary/Upper Respiratory	13.3% (29/218)	28.9% (22/76)	5.2% (11/211)	2.7% (2/75)	16.5% (36/218)	30.3% (23/76)
Renal	3.2% (7/218)	9.2% (7/76)	4.7% (10/211)	4.0% (3/75)	7.8% (17/218)	11.8% (9/76)
Vascular	12.4% (27/218)	3.9% (3/76)	6.6% (14/211)	4.0% (3/75)	18.3% (40/218)	7.9% (6/76)
Wound	6.4% (14/218)	5.3% (4/76)	3.3% (7/211)	6.7% (5/75)	9.6% (21/218)	11.8% (9/76)

2.4 Device- and Procedure-Related Adverse Events: The following section lists Adverse Events (Major, Severe and non-Severe) by relationship to the device or procedure. The relationship of the event to the device or procedure was adjudicated by the sites themselves without DMC overview. The sites did not adjudicate the relationship of every event and as a result, the total number of events listed in these tables is slightly less than the full total number of events listed in Table 20, Table 27 and Table 28.

Device- and Procedure-Related Major Adverse Events

Table 29 and Table 30 list Major Adverse Events by relationship to device and procedure respectively.

Table 29 Device-Related Major Adverse Events through 12 Months

% (n/N) AE Type	Aorfix™ ITT[1] N=218	
	0-30 Days	0-365 Days
Blood loss requiring transfusion	2.3% (5/218)	2.3% (5/218)
Aneurysm rupture	0	0.5% (1/218)
Graft occlusion	1.8% (4/218)	2.3% (5/218)
Graft thrombosis	0.5% (1/218)	0.9% (2/218)

[1]**Investigational sites reported only procedure-related MAEs**

Table 30 Procedure-Related Major Adverse Events through 12 Months

% (n/N) AE Type	0-30 Days		0-365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=218	COS ITT N=76
EBL requiring transfusion	4.6% (10/218)	9.2% (7/76)	4.6% (10/218)	9.2% (7/76)
Congestive heart failure (CHF)	0.9% (2/218)	0	0.9% (2/218)	0
Pulmonary failure	0.5% (1/218)	1.3% (1/76)	0.5% (1/218)	1.3% (1/76)
Renal failure	0.9% (2/218)	1.3% (1/76)	0.9% (2/218)	1.3% (1/76)
Bowel ischemia	0.5% (1/218)	0	0.5% (1/218)	0
Surgical wound complication	4.1% (9/218)	3.9% (3/76)	4.6% (10/218)	6.6% (5/76)
Aneurysm rupture	0% (0/218)	0	0.5% (1/218)	0

% (n/N) AE Type	0-30 Days		0-365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=218	COS ITT N=76
Graft occlusion	0.5% (1/218)	1.3% (1/76)	0.5% (1/218)	1.3% (1/76)
Graft thrombosis	0.9% (2/218)	0	0.9% (2/218)	0
Need for device replacement or revision	0.5% (1/218)	0	0.9% (2/218)	0

Device- and Procedure-Related Serious Adverse Events

Table 31 and Table 32 list Serious Adverse Events in relation to the device and the procedure.

Table 31 Device-Related Serious Adverse Events

% (n/N) AE Category	0 to 30 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=218	COS ITT N=76
SAEs	10.6% (23/218)	0	13.3% (29/218)	0
Bleeding	3.2% (7/218)	0	3.7% (8/218)	0
Other	0.9% (2/218)	0	0.9% (2/218)	0
Renal	1.4% (3/218)	0	1.4% (3/218)	0
Vascular	6.9% (15/218)	0	10.1% (22/218)	0

Table 32 Procedure-Related Serious Adverse Events

% (n/N) AE Category	0 to 30 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=218	COS ITT N=76
SAEs	25.7% (56/218)	34.2% (26/76)	26.1% (57/218)	38.2% (29/76)

% (n/N) AE Category	0 to 30 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=218	COS ITT N=76
Bleeding	14.2% (31/218)	25.0% (19/76)	14.2% (31/218)	25.0% (19/76)
Cardiac	2.8% (6/218)	5.3% (4/76)	2.8% (6/218)	5.3% (4/76)
Gastrointestinal	2.3% (5/218)	5.3% (4/76)	2.3% (5/218)	6.6% (5/76)
Neurologic	0.5% (1/218)	0	0.5% (1/218)	0
Other	2.3% (5/218)	0	2.3% (5/218)	0
Pulmonary/Upper Respiratory	2.3% (5/218)	7.9% (6/76)	2.3% (5/218)	7.9% (6/76)
Renal	4.6% (10/218)	7.9% (6/76)	4.6% (10/218)	9.2% (7/76)
Vascular	6.4% (14/218)	5.3% (4/76)	7.3% (16/218)	5.3% (4/76)
Wound	2.8% (6/218)	1.3% (1/76)	2.8% (6/218)	2.6% (2/76)

Device- and Procedure-Related Adverse Events Excluding SAEs

Table 33 and Table 34 list non-Serious Adverse Events by relationship to device and procedure.

Table 33 Adverse Events Excluding SAEs through 12 Months, Device Related

% (n/N) AE Category	0 to 30 Days		31 to 365 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=211	COS ITT N=75	Aorfix™ ITT N=218	COS ITT N=76
AEs (excl SAE)	5.5% (12/218)	0	2.4% (5/211)	0	7.8% (17/218)	0
Bleeding	0.5% (1/218)	0	0	0	0.5% (1/218)	0
Neurologic	0	0	0.5% (1/211)	0	0.5% (1/218)	0

% (n/N) AE Category	0 to 30 Days		31 to 365 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=211	COS ITT N=75	Aorfix™ ITT N=218	COS ITT N=76
Other	1.4% (3/218)	0	0	0	1.4% (3/218)	0
Renal	0.5% (1/218)	0	0.5% (1/211)	0	0.9% (2/218)	0
Vascular	3.7% (8/218)	0	1.4% (3/211)	0	5.0% (11/218)	0

Table 34 Adverse Events Excluding SAEs through 12 Months, Procedure Related

% (n/N) AE Category	0 to 30 Days		31 to 365 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=211	COS ITT N=75	Aorfix™ ITT N=218	COS ITT N=76
AEs (excl SAE)	47.2% (103/218)	67.1% (51/76)	10.0% (21/211)	10.7% (8/75)	50.0% (109/218)	69.7% (53/76)
Bleeding	21.1% (46/218)	26.3% (20/76)	0.5% (1/211)	0	21.1% (46/218)	26.3% (20/76)
Cancer	0	0	0	0	0	0
Cardiac	16.1% (35/218)	18.4% (14/76)	0	0	16.1% (35/218)	18.4% (14/76)
Edema	5.0% (11/218)	5.3% (4/76)	0	0	5.0% (11/218)	5.3% (4/76)
Gastrointestinal	16.5% (36/218)	27.6% (21/76)	0.5% (1/211)	4.0% (3/75)	16.5% (36/218)	30.3% (23/76)
Genitourinary	6.4% (14/218)	1.3% (1/76)	0	1.3% (1/75)	6.4% (14/218)	2.6% (2/76)
Infection	3.2% (7/218)	3.9% (3/76)	0.5% (1/211)	1.3% (1/75)	3.7% (8/218)	3.9% (3/76)
Neurologic	5.5% (12/218)	10.5% (8/76)	0.9% (2/211)	0	6.4% (14/218)	10.5% (8/76)
Orthopedic	4.1% (9/218)	0	0	0	4.1% (9/218)	0
Other	22.9% (50/218)	34.2% (26/76)	1.9% (4/211)	2.7% (2/75)	23.4% (51/218)	35.5% (27/76)

% (n/N) AE Category	0 to 30 Days		31 to 365 Days		0 to 365 Days	
	Aorfix™ ITT N=218	COS ITT N=76	Aorfix™ ITT N=211	COS ITT N=75	Aorfix™ ITT N=218	COS ITT N=76
Pulmonary/Upper Respiratory	9.6% (21/218)	17.1% (13/76)	0	0	9.6% (21/218)	17.1% (13/76)
Renal	3.2% (7/218)	9.2% (7/76)	1.9% (4/211)	0	5.0% (11/218)	9.2% (7/76)
Vascular	7.3% (16/218)	3.9% (3/76)	1.9% (4/211)	0	9.2% (20/218)	3.9% (3/76)
Wound	6.0% (13/218)	5.3% (4/76)	3.3% (7/211)	4.0% (3/75)	9.2% (20/218)	9.2% (7/76)

2.5 Safety Endpoints Compared with SVS Lifeline Registry Outcomes: Per the protocol, endpoints from the Aorfix™ arm of the study were also compared with outcomes found in the SVS Lifeline Registry. Demographics of the subject groups can be found in Table 35 to Table 38 and in Zwolak et al, 2008. Results for safety endpoints are listed in Table 39 and Table 40.

Table 35 Subject Demographics vs SVS

N Mean ±STD % (n/N)	Aorfix™ ITT N=218	SVS N=323
Mean Age		
Age	n=218 75.6 ±7.51	n=323 69.7 ± 7.41
Min – Max	52 - 94	41 – 86
Age Category▲▲		
≤55 years	0.5% (1/218)	2.2% (7/323)
56-65 years	11.5% (25/218)	25.1% (81/323)
66-75 years	35.3% (77/218)	49.2% (159/323)
76-85 years	46.3% (101/218)	23.2% (75/323)
≥86 years	6.4% (14/218)	0.3% (1/323)
Gender		
Male	71.1%▲ (155/218)	83.3% (269/323)
Female	28.9%▲ (63/218)	16.7% (54/323)

▲indicates difference between each Aorfix™group and the SVS population p≤0.05
▲▲ The distribution of ages is significantly different from SVS for all Aorfix™ subgroups

Table 36 Ethnicity vs SVS

% (n/N) Subject Ethnicity	Aorfix™ ITT N=218	SVS N=323[1]
White, non-Hispanic	92.2% (201/218)	94.9% (244/257)
Non-White	7.8% (17/218)	5.1% (13/257)

[1] - 66 SVS subjects were missing race information.
There is no significant difference between the Aorfix™ ITT and the SVS populations assessed by Fisher's Exact Test.

Significant differences in baseline medical history are shown in Table 37. The Aorfix™ ITT population had elevated rates of arrhythmia (21.6% vs. 13.9%), congestive heart failure (12.6% vs. 6.5%), hypertension (85.3% vs. 70.6%) myocardial infarction (24.5% vs. 3.3%) and renal disease (14.3% vs. 3.1%). SVS subjects had elevated rates of peripheral arterial occlusive disease (18.0% vs. 10.1%) and alcohol abuse (8.5% vs. 3.2%). Cardiovascular disease was also significantly (66.6% vs. 0%) because this was not a single category collected for Pythagoras patients.

Table 37 Baseline Medical History vs SVS

% n/N Prior Condition	Aorfix ITT N=218	SVS N=323
Cardiovascular disease[1]	0	66.6%▲ (215/323)
Arrhythmia	21.6%▲ (47/217)	13.9% (45/323)
Congestive Heart Failure	12.6% ▲ (27/214)	6.5% (21/323)
Coronary Artery Disease	45.8% (99/216)	53.3% (172/323)
Family History of AAA Disease	22.4% (43/192)	17.9% (38/212)
History of Stroke or TIA	13.4% (29/216)	13.6% (44/323)
Hypertension	85.3%▲ (185/217)	70.6% (228/323)
Myocardial Infarction	24.5%▲ (53/216)	3.3% (8/243)
Peripheral arterial occlusive disease	10.1% (21/207)	18.0%▲ (58/323)
Valvular Disease	10.6% (23/218)	8.5% (15/177)
Alcohol abuse	3.2% (7/217)	8.5%▲ (18/212)
Cancer	29.5% (64/217)	23.6% (50/212)
Diabetes	17.5% (38/217)	12.7% (41/323)
Liver disease	4.6% (10/218)	3.4% (5/146)
Pulmonary insufficiency	31.8% (68/214)	26.9% (87/323)
Renal Disease[2,3]	14.3%▲ (31/217)	3.1% (10/323)
Tobacco use	87.2% (190/218)	88.2% (285/323)

[1] Cardiovascular disease consists of having any of the following: angina, CAD, PVD, cardiac intervention CABG or PTA), MI in past 6 months, CHF, or peripheral vascular disease. Not all of these were assessed in Aorfix™ subjects.
[2] Chronic Renal Failure only available in SVS group.
[3] Renal disease is defined as renal failure or renal insufficiency and is only available in Aorfix™ ITT and Open ITT groups
▲Denotes difference between Aorfix™ ITT and SVS populations is different, $p \leq 0.05$ generated from Fisher's Exact Test.

Table 38 lists the distribution of aneurysm diameters. The Aorfix™ <60° group had slightly smaller aneurysms than SVS, reaching significance. The Aorfix™ ≥ 60° group had a distribution that was slightly larger than the SVS population but did not reach significance.

Table 38 Baseline Aneurysm Diameters vs SVS

% (n/N) Diameter(mm)	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	SVS[1] N=323[2]
< 30	0	0.7% (1/151)	0.5% (1/218)	0
30 to < 40	0% (0/0)	1.3% (2/151)	0.9% (2/218)	1.7% (5/292)
40 to < 50	38.8% (26/67)	14.6% (22/151)	22.0% (48/218)	17.8% (52/292)
50 to < 60	40.3% (27/67)	47.0% (71/151)	45.0% (98/218)	40.1% (117/292)
60 to < 70	14.9% (10/67)	20.5% (31/151)	18.8% (41/218)	22.6% (66/292)
70 to < 80	4.5% (3/67)	10.6% (16/151)	8.7% (19/218)	11.6% (34/292)
80 to < 90	1.5% (1/67)	3.3% (5/151)	2.8% (6/218)	4.1% (12/292)
≥ 90	0	2.0% (3/151)	1.4% (3/218)	2.1% (6/292)
Significance[3]	▲			N/A

[1] from Zwolak, 2008
[2] Diameter information was unavailable in 31 subjects
[3] Mantel-Haenszel test based on distribution of aneurysm diameters
▲Denotes a difference from SVS, p≤0.05.

Table 39 lists Pythagoras freedom from SVS MAEs compared with the Lifeline Registry results at 30 days and 12 months. Table 40 compares Pythagoras all-cause mortality with the Lifeline Registry.

Table 39 Freedom from SVS-MAE at 30 Days and 12 Months vs SVS

% (n/N) [95% CI]	Aorfix™ <60° N=67	Aorfix™ ≥60° N=151	Aorfix™ ITT N=218	SVS N=323
Freedom from any SVS-MAE within 30 days	92.5% (62/67) [83.4% - 97.5%]	81.5% (123/151) [74.3% - 87.3%]	84.9% (185/218) [79.4%-89.4%]	56.3% (182/323) [50.8% - 61.8%]
Freedom from any MAE within 12 months	88.1% (59/67) [77.8% - 94.7%]	76.2% (115/151) [68.6% - 82.7%]	79.8% (174/218) [73.9% -84.9%]	54.5% (176/323) [48.9% - 60.0%]

Table 40 All Cause Mortality Free at 12 Months vs SVS

% (n/N) [95% CI]	Aorfix™ ITT N=218	Aorfix™ ≥60° N=151	Aorfix™ <60° N=67	SVS N=323
All Cause Mortality Free Rate at 365 Days	94.8% 205/218 [90.0%-96.8%]	93.7% (140/151) [87.3%-96.3%]	97.0% (65/67) [89.6% - 99.6%]	93.5% (302/323) [90.2%-95.9%]

3. Effectiveness Results

3.1 Composite Effectiveness Endpoint: Table 41 provides the proportion of subjects in the Aorfix™ group and in the post-hoc analysis to reach the primary effectiveness composite endpoint at 12 months. The analysis is limited by including all data from 12 months as well as from later time points when 12 month data was not available for a particular endpoint. With this imputation, the composite endpoint was achieved by 89% (Lower Bound: 80.1%) subjects in the pre-defined analysis group (60° to 90°) and by 90.7% (Lower Bound: 84.6%) subjects in the post-hoc defined all-angle group.

Table 41 Primary Effectiveness at 12 Months

% (n/N) [95% CI][2] Primary Effectiveness	Aorfix™ <60° As Treated N=67	Aorfix™ ≥60° As Treated N=143	Aorfix™ As Treated N=210
Composite endpoint success	92.5% (37/40) [79.6%, 98.4%]	90.0% (90/100) [82.4%, 95.1%]	90.7% (127/140) [84.6%, 95.0%]
Endoleak Type I or III	0	1.9% (2/105)	1.3% (2/150)
Fracture in fixation zone (Hooks)	6.4% (3/47)	6.1% (7/114)	6.2% (10/161)
Migration (>10mm)	0	1.7% (2/119)	1.2% (2/172)

A tipping point analysis was also conducted to assess the impact that missing data had on the results. Of the 70 total subjects who are not evaluable at 12 months the tipping imputation results in a failure on the primary effectiveness endpoint when 19 (27%) are imputed as failures. This is nearly 3 times the rate actually seen in the group with full data and suggests that the missing data is not biasing the results.

Migration (Core Lab)

There were 2 cases of stent graft migration in the Aorfix™ population through 12 months. One subject is described below because a hook fracture was detected. In the second case of migration, the diameter of the aorta at the distal renal increased from 28mm post-operatively to 35mm at 12m. The aortic neck angle was 75°. The subject received a 31mm proximal diameter graft. There was no endoleak, sac diameter was stable at 12 months and there was a sac volume increase of 10.4%.

Fracture (Core Lab)

Ten subjects were identified with hook fracture. Following an analysis of these subjects at 12 post-operative months, there was an association with major, rapid neck dilatation in the majority of cases. Fractures were associated with subjects where the proximal sealing zone (that part of the aorta in which the proximal part of the stent graft lies) had dilated rapidly (mean 4.85mm) in the first 12 months. In many cases, this dilation was associated with the device having been landed more than 1cm below the distal renal artery, usually in an attempt to use an adequate infra-renal proximal landing zone for the device. In anatomies with an ectatic peri-renal aorta with a short, narrower infra-renal

zone prior to the aneurysmal sac forming distally, the dimensions of the shorter narrower zone (the isthmus) appear to be particularly unstable as it dilates rapidly to match the dimensions of the aorta above and below these zones.

Neck dilation is more marked in subjects having neck angles of 60° and above with a mean increase of nearly 8mm in the juxta-renal (1mm infrarenal) aorta at 12 months in this group. Those subjects having a neck angle less than 60° experienced neck dilation of just over 3mm in the same period (Table 42). Of note, the bottom of the proximal aortic neck has dilated more markedly than the top in all angle groups. The fishmouth of the Aorfix™ is generally placed trans-renally, ie at the top of the aortic neck. As a result of the four closely spaced wire rings at the fishmouth, the radial force in the fishmouth is approximately four times that of the rest of the graft. Therefore the larger dilation seen at the bottom of the aortic neck occurs where there is low radial force from the graft while the lower dilation at the top of the neck occurs where the radial force of the graft is four times higher. This observation indicates that the dilation is not a consequence of radial force.

Table 42 Neck diameter changes from pre-op to 12 month post-op CT

n **Mean** **± SD**	**Aorfix™** **<60°** **N=67**	**Aorfix™** **≥60°** **N=151**	**Aorfix™** **ITT** **N=218**
Dilation in Proximal Neck Diameter 1mm infra-renal (%)	n=57 3.26 ± 8.06	n=126 7.88 ± 10.51	n=183 6.44 ± 10.02
Dilation in Proximal Neck Diameter 15mm infra-renal (%)	n=57 10.48 ± 11.37	n=126 14.94 ± 18.80	n=183 13.55 ± 16.93

The most likely consequences of hook fracture are migration and Type Ia endoleak. The only subject having a Type Ia endoleak at 12 months did not have a fractured hook. Of the 2 subjects with migration, 1 subject had a fractured hook. This subject had a neck angle of 102°, a neck length of 12mm and a neck diameter that dilated from 27mm to 30mm at 12 months. The subject received a 28mm proximal diameter graft. Sac diameter reduced 18mm from 77mm to 59mm in the same period.

Note that 2 stent-ring fractures were identified in the distal region of the aortic component. The fractures have not been associated with any complications or interventions.

A revised wire specification was introduced during 2010. All hook fractures occurred in wire manufactured prior to this date.

Endoleak at 30 Days and at 12 months

Table 43 shows all Types of endoleaks as identified by the core lab at 1 month and 12 months for the Aorfix™ population. There were 2 Type I and zero (0) Type III endoleaks at 1 month, and 1 Type I and 1 Type III at 12 months.

Table 43 Endoleak Rates (Core Lab Assessed)

% (n/N) Endoleak	Aorfix™ <60° As Treated N=67		Aorfix™ ≥60° As Treated N=143		Aorfix™ As Treated N=210	
Time point	**30 Days**	**12 months**	**30 Days**	**12 months**	**30 Days**	**12 months**
Endoleak Type Ia▲▲	0	0	1.8% (2/113)	1.0% (1/100) ▲	1.2% (2/163)	0.7% (1/143)
Endoleak Type II	16.0% (8/50)	14.0% (6/43)	17.7% (20/113)	13.0% (13/100)	17.2% (28/163)	13.3% (19/143)
Endoleak Type III	0	0	0	1.0% (1/100)	0	0.7% (1/143)
Endoleak Type IV	0	0	0	0	0	0
Indeterminate	2.0% (1/50)	0	0	3.0% (3/100)	0.6% (1/163)	2.1% (3/143)

▲The Type I endoleak identified at 12 months was seen in a subject who received a non-contrast CT at earlier follow-up.
Note that grayed table cells indicate values of zero (0).
▲▲ The Core lab did not identify any Type Ib endoleaks although 2 Type Ib endoleaks were identified and treated by sites.

Table 44 provides details of the 2 subjects with Type I and Type III endoleaks at 12 months.

Table 44 Narrative details of subjects with Type I or Type III endoleak at 12 months

Angle (°)	Narrative	Related Protocol MAE	Endoleak Type
94	Pre-op neck length measurement by core-lab of 9mm and diameter of 20.5mm. 28mm proximal diameter graft placed juxtarenally. Endoleak seen from first post-op scan without secondary intervention.	None	Type Ia
82	Small endoleak seen at bottom of sac adjacent to connection with distal extender. Leg re-lined with a competitor stent graft limb extending to the external iliac but endoleak persisted at reduced level. Lumbar Type II was then coil occluded with successful exclusion of endoleak.	None	Type III

3.2 Secondary Analyses:

Changes in Aneurysm Size from 30 Days to 12 months

Changes in sac diameter are used to assess the success of exclusion of the aneurysm sac. Volume measurements can only be performed by software but are regarded as providing greater sensitivity to changes in sac size.

Table 45 shows the change in aneurysm diameter and volume as identified by Core Lab from 1 month to 12 months.

- 1 sac increased in diameter as a result of a Type II endoleak. It also increased in volume.
- 1 sac increased in diameter without endoleak being detected. It did not increase in volume.
- 9 sacs increased in volume as a result of 8 Type II endoleaks and 1 Type I endoleak.
- 10 sacs increased in volume without endoleak being detected.

In the Aorfix™ population, 44.1% of Aorfix™ ≥60° group showed sac diameter shrinkage. The sensitive sac volume measurements showed an increase in volume of the sac in 11.9% patients and, as well as including the two patients with an increase in diameter, it also included volume increases as a consequence of Type II endoleak.

Table 45 Changes in Size of Aneurysm at 12 Months

% (n/N) Measure	Change	Aorfix™ <60° As Treated N=67	Aorfix™ ≥60° As Treated N=143	Aorfix™ As Treated N=210
Diameter	≥5 mm Shrinkage	36.7% (18/49)	44.1% (49/111)	41.9% (67/160)
	No Diameter Change	63.3% (31/49)	54.1% (60/111)	56.9% (91/160)
	≥5 mm Growth	0	1.8% (2/111)	1.2% (2/160)
Volume	≥5% Shrinkage	71.4% (35/49)	73.0% (81/111)	72.5% (116/160)
	No Volume Change	18.4% (9/49)	14.4% (16/111)	15.6% (25/160)
	≥5% Growth	10.2% (5/49)	12.6% (14/111)	11.9% (19/160)

Table 46 provides details of the 2 patients with sac diameter increases > 5mm at 12 months.

Table 46 Narrative details of subjects with sac diameter increase >5mm at 12 months

Angle	Narrative	Secondary intervention	Protocol MAE
97	Sac increased 5.2mm in diameter to 73.3mm. Subject with poor renal function did not have contrast enhance CT post-operative. Highly angled neck with significant volume reduction of 19.6% at 12 months. Some remodeling of graft has taken place which may explain increased diameter.	None	None
87	Sac increased 9.5mm in diameter to 84.6mm. Six months post-operative a successful coil embolization of Type II endoleak was performed.	Successful Embolization Of AAA Sac	Need for Device Replacement or Revision

3.3 Secondary Procedures through 12 months: In the first 12 months, 34 subjects required a secondary procedure be performed. The DMC adjudicated those which were device-related (Table 47) from those which were related to the procedure or the patient's underlying condition (Table 48). A total of 7 procedures were associated with treatment

of a loss of stent graft leg patency and 6 procedures involved treatment of a loss of renal artery patency. Six (6) procedures involved treatment of Type II endoleaks and 6 procedures treated occlusive disease of the access vessels. Related Protocol MAEs are as reported by the investigational sites. Nineteen (19) were reported for the 34 secondary procedures. Secondary procedures were defined as surgical procedures requiring a separate anaesthesia to that induced for the index procedure.

Adjunctive procedures (listed inTable 49) were performed during the index procedure but were additional to the deployment of the stent graft.

Table 47 Secondary Procedures Related to the Device (DMC Adjudication)

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Procedures to Treat Graft Leg Loss of Patency						
Stenting of Graft						
Balloon-Expandable Stent	Graft Leg	Stenosis of Graft	None	None	The 30 day follow-up CT suggested kinking or stenosis of the right, ipsilateral limb. A stent was placed in the right common iliac artery in the region of stenosis. The terminal aorta had a diameter of 20mm and is potentially associated with the reduction in lumen.	Compressed gate
Self-Expanding Stent	Graft Leg	Stenosis of Graft	Graft Occlusion	None	An occluded right iliac was detected 11 days post-operative. A narrow terminal aorta (16.5mm) was identified as having caused bilateral lumen reduction and the lumens of both legs which were treated with angioplasty and kissing stents.	Compressed gate
Fem-Fem bypass						
Vascular Graft	Graft Leg and Distal Extension	Occlusion of Graft	Graft Occlusion	None	During the index procedure, a distal extender to the left limb was placed. The proximal end of the extender was partially opened due to excess over-size or inadequate ballooning and at 1 month follow-up a fem-fem bypass was performed to resolve the resultant occlusion.	Proximal end of distal extender not fully dilated
Vascular Graft	Graft Leg	Occlusion of Graft	Need for Device Replacement or Revision	Graft Thrombosis	A thrombosed common iliac was found 5 weeks after the index procedure. The ectatic iliac was sized to receive a 20mm short contralateral limb. A 20mm extension was placed to the iliac bifurcation which was 11mm in diameter and gave rise to subsequent occlusion. A fem-fem bypass was performed to restore flow.	Excess oversize
Vascular Graft	Graft Leg and Distal Extension	Occlusion of Graft	Graft Occlusion	None	During the index procedure, a distal extender to the right limb was placed. The proximal end of the extender was partially opened due to excess over-size or inadequate ballooning and at 6 month follow-up a fem-fem bypass was performed to resolve the resultant claudication.	Proximal end of distal extender not fully dilated
Lysis and Angioplasty						
None	Graft Leg and Distal Extension	Occlusion of Graft	None	None	At index procedure a primary graft with a 12mm distal right diameter was implanted but extended with a 20mm diameter distal extender. This side thrombosed one month post-operatively and was successfully treated with lysis and angioplasty. Distal extenders are designed to be used inside grafts of their own diameter.	Mismatched size of - distal extender and graft leg
Procedures to Treat Renal Artery Loss of Patency						
Stenting Renal Artery						
Balloon-Expandable Stent	Renal Artery	Renal Part Covered by Graft	None	Bowel Ischemia	During the index procedure, a initial Type I endoleak on primary graft resolved by placement of proximal cuff. Right renal artery was covered by the cover and flow restored by placement of a stent.	Flow restoration

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Balloon-Expandable Stent	Renal Artery	Prophylaxis	None	Excessive Bleeding Requiring Transfusion	After an initial low placement of the primary graft, a proximal cuff was placed. Bilateral renal artery patency was demonstrated but at 7months post op, renal stents were placed prophylactically to limit renal encroachment.	Prophylaxis
Balloon-Expandable Stent	Renal Artery	Stenosis of Renal Artery	None	Surgical Wound Complication	During the index procedure, a initial Type I endoleak on primary graft resolved by placement of proximal cuff. Two days post-op, elevated creatinine prompted renal angiography and the right renal artery was stenosed. This was resolved by placement of a stent.	Flow restoration
Balloon-Expandable Stent	Renal Artery	Prophylaxis	Need for Device Replacement or Revision	None	At 30 days follow up encroachment of the graft on the right renal artery was prophylactically treated successfully with a renal stent.	Prophylaxis
None	Renal Artery	Renal Part Covered by Graft	None	None	During the index procedure a competitor proximal cuff was placed which partially covered the left renal artery. It was not successfully recanalized.	Observation
Procedures to Treat Other Complications						
Stenting of Graft						
Balloon-Expandable Stent	Aortic Neck	Type Ia Endoleak	Need for Device Replacement or Revision	Renal Failure Requiring Dialysis	Seven days post-operative a suspected Type I endoleak was treated with a balloon expandable stent. During deployment, the aorta was torn by the stent and open repair of the tear was successfully completed.	Type Ia
Extension of Stent Graft						
Stent Graft	Graft Leg	Type Ib Endoleak	Need for Device Replacement or Revision	None	During the index procedure the right limb endograft was found to be too short and could not be satisfactorily extended. Two months postoperative, a long extension component was implanted successfully.	Type Ib
Stent Graft	Graft Leg	Type Ib Endoleak	Need for Device Replacement or Revision	None	Six months post-operative a distal extension cuff was successfully implanted to correct a Type Ib distal endoleak.	Type Ib
Conversion to Open Repair						
Vascular Graft	Aorta and Iliac Arteries	Total Graft Occlusion	Need for Device Replacement or Revision	None	The subject suffered a complete graft occlusion 2 weeks post-operative and was bypassed with an axilo-bifemoral graft. Subsequent to complete occlusion of the bypass graft, the subject was diagnosed with a hypercoagulable state (Factor II gene modification) and was managed medically.	Coagulation disorder

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Exclusion of Hypogastric Aneurysm						
Stent Graft	Common Iliac Bifurcation	Hypogastric Aneurysm	None	None	Eight months post-operative, a right sided hypogastric artery aneurysm was enlarging. A covered stent was used to extend the AAA stent graft into the external iliac artery to exclude the hypogastric. The procedure was unsuccessful.	Other vascular
Implantation of Venous Filter						
Venous Filter	Inferior Vena Cava	DVTs	None	Graft Thrombosis	Four days post-operative the subject suffered DVTs and a venous filter was placed.	Other vascular
Stenting for Dissection						
Self-Expanding Stent	External Iliac Artery	Dissection	None	Pulmonary Failure Requiring Intubation	Two weeks post-operatively stenting was performed to treat a left external iliac dissection.	Access vessel

Table 48 Summary of Secondary Procedures Related to the Index Procedure or the Patient's Underlying Condition (DMC Adjudication)

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Procedures to Treat Graft Leg Loss of Patency						
Lysis and Angioplasty						
None	Graft Leg	Occlusion of Graft	Graft Thrombosis	Surgical Wound Complication	Occlusion of the ipsilateral leg was treated one month post-operative with jetting and TPA. The subject had a 41 mm long proximal neck in which the flow divider of the graft lay. The ipsilateral limb was thereby compressed by the contralateral gate in this unusual anatomy.	Compressed gate
Procedures to Treat Renal Artery Loss of Patency						
Stenting Renal Artery						
Balloon-Expandable Stent	Renal Artery	Stenosis of Renal Artery	None	None	Previously placed giant balloon expandable stent to treat Type I endoleak. Renal ischemia diagnosed 6 months post-op and successfully treated with renal stent	Flow restoration

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Procedures to Treat Type II Endoleaks						
Branch Vessel Embolization						
Embolization Coil	Lumbar Artery	Type II Endoleak	Need for Device Replacement or Revision	None	At six months post-operative, a Type II endoleak was successfully coil occluded.	Type II
Embolization Coil	Lumbar Artery	Type II Endoleak	Need for Device Replacement or Revision	None	Nine months post-operative a coil embolization of a persistent Type II endoleak was successfully performed.	Type II
Embolization Coil	Lumbar Artery	Type II Endoleak	Need for Device Replacement or Revision	None	Six months post-operative successful embolization of right sided lumbar endoleak Type II.	Type II
Embolization Coil	Lumbar Artery	Type II Endoleak	Need for Device Replacement or Revision	None	Six months post-operative un-successful embolization of left sided lumbar endoleak Type II.	Type II
Embolization Coil	Lumbar Artery	Type II Endoleak	Need for Device Replacement or Revision	Excessive Bleeding Requiring Transfusion	Six months post-operative a successful coil embolization of Type II endoleak was performed.	Type II
Embolization Coil	Lumbar Artery	Type II Endoleak	Need for Device Replacement or Revision	Cardiac Arrest	Six months post-operative a successful coil embolization of Type II endoleak was performed.	Type II
Procedures to Treat Access Vessels						
Endarterectomy						
None	Femoral Artery	Stenosis of Native Vessel	None	Graft Occlusion	Two days post-operative, diminished ABIs were treated by re-intervention for left common femoral endarterectomy and patch angioplasty.	Access vessel disease

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
None	Femoral Artery	Occlusion of Native Vessel	None	Excessive Bleeding Requiring Transfusion	Six weeks post-operative a successful common femoral artery endarterectomy was performed.	Access Vessel
Angioplasty						
None	Common Iliac	Dissection	None	None	30 day post-operative a dissection of the left common iliac artery was successfully treated with balloon angioplasty.	Access Vessel
Fem-Fem bypass						
Vascular Graft	External Iliac Artery	Occlusion of Native Vessel	None	None	Three months postoperatively the right external iliac artery occluded. This was successfully treated with a fem-fem bypass.	Access Vessel
Stenting for Dissection						
Balloon-Expandable Stent	External Iliac Artery	Stenosis of Native Vessel	Graft Thrombosis	None	During the index procedure the left limb was extended past an aneurysmal common iliac artery into the external iliac. Following severe leg pain, left common femoral and iliac thrombosis was diagnosed arising from plaque in the left femoral with dissection retrograde into left common iliac. Kinking or lumen reduction in the left leg of graft was observed. Treatment was thrombectomy and stent placement, post-operative but on the day of the procedure.	Native vessel stenosis
Procedures to Treat Other Complications						
Artery Reconstruction						
None	Femoral Artery	Femoral Pseudoaneurysm	None	None	Five months post-operative a successful repair of right common femoral pseudoaneurysm was performed.	Access vessel
Wound Debridement						
None	Wound	Slow Wound Healing	Surgical Wound Complication	None	At 30 day post-operative, bilateral groin wound debridement was performed.	Wound
Wound Drainage						

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
None	Wound	Wound Seroma	Surgical Wound Complication	None	Two weeks post-operative a bilateral groin seroma washout and wound vac placement was successfully performed.	Wound

3.4 Adjunctive Procedures Performed at Index Procedure: The majority of this section addresses the As Treated population (N=210). The following discussion of adjunctive procedures performed during the index procedure includes subjects that were not successfully implanted with Aorfix. It therefore addresses the Intention To Treat population (N=218) so as to include all procedures involving intra-operative conversions and access failures. These are indicated by a '▲' symbol; note that only 7 subjects are indicated because no attempt was made to gain access in one subject after review of the on-table arteriogram.

Adjunctive procedures (listed inTable 49, as reported by investigational sites) were performed during the index procedure but were additional to the deployment of the stent graft. Twenty-one (21) were reported; stenting of 1 stenosed graft leg, 2 renal arteries and attempted stenting of a third took place. Access complications are reported in 8 subjects and intra-operative open conversion is reported 3 times.

Delivery system tip entrapment is reported twice, as a complication of access, while extending a stent graft into a narrow external iliac artery and involved detachment of the tip on one occasion. Since these events, the design of the tip has been changed to reduce its profile and the method of attaching it has been re-specified.

Table 49 Adjunctive Procedures Performed at Index Procedure

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Adjunctive Treatment of Graft Leg Loss of Patency						
Adjunctive Stenting of Graft at Index Procedure						
Self-Expanding Stent	Graft Leg	Stenosis of Graft	None	None	During the index procedure, compression of the ipsilateral limb (left) by contralateral socket was noted. 2 x self expanding stents were placed into Ipsilateral limb. Compression and increasing claudication continued and a fem-fem bypass performed two years post-op.	Compressed gate
Adjunctive Treatment of Renal Artery Loss of Patency						
Adjunctive Stenting Renal Artery at Index Procedure						
Balloon-Expandable Stent	Renal Artery	Renal Part Covered by Graft	None	None	During the index procedure, slight encroachment of the graft on the left renal artery was observed and treated prophylacticly with a stent.	Prophylaxis
Self-Expanding Stent	Renal Artery	Stenosis of Renal Artery	None	None	At index procedure partial stenosis of the right renal artery was seen and treated with a stent.	Prophylaxis
None	Renal Artery	Renal Part Covered by Graft	None	None	During the index procedure a proximal cuff was placed which partially covered the right renal artery. It was not successfully recanalized but attempts caused dissection and subsequent thrombosis.	Unsuccessful Renal Cannulation
Adjunctive Treatment of Type II Endoleaks						
Adjunctive Branch Vessel Embolization at Index						
Embolization Coil	Lumbar Artery	Type II Endoleak	None	None	Performed at Index Procedure	Type II
Adjunctive Treatment of Access Complications						
Access Failure						

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Multiple Balloon-Expandable and Self-Expanding Stents	Aorta and Iliac Arteries	Access Failure	Excessive Bleeding Requiring Transfusion	None	During the index procedure, narrow access vessels were stented in an unsuccessful attempt to gain access for the stent graft delivery system. The patient was treated with an open aneurysm repair.	Attempted Access▲
None	Aorta and Iliac Arteries	Access Failure	Excessive Bleeding Requiring Transfusion	None	During the index procedure the subject's left iliac system was very tortuous (tortuosity index = 2.0). The main body delivery system was able to reach the intended delivery site but did not operate and the graft could not be deployed. The AAA was treated by open surgical repair.	Extreme iliac tortuosity▲
Adjunctive Revision to Competitor EVAR						
Stent Graft	Aorta and Iliac Arteries	Access Failure	None	None	During the index procedure, the delivery system could not be introduced and the patient was treated with a competitor graft.	Attempted Access▲
Adjunctive Stenting Access Vessel at Index						
Multiple Balloon-Expandable and Self-Expanding Stents	External Iliac Artery	Access Improvement	Excessive Bleeding Requiring Transfusion	None	During the index procedure, narrow access vessels were stented with peripheral and covered stents in an unsuccesful attempt to gain access for the stent graft delivery system. AAA repair was abandoned in this patient as no acceptable alternative treatments could be found.	Attempted Access▲
Adjunctive Fem-Fem bypass at Index						
Vascular Graft	External Iliac Artery	Bypass Embolized Delivery System Tip	None	None	During the index procedure the stent graft was extended to the left external iliac artery. On removal of the delivery system the tip of the delivery system detached and remained permanently lodged in te left external iliac artery. A fem-fem bypass was performed to restore flow to the occluded limb.	Extension of graft to undersized external iliac
Adjunctive Artery Reconstruction						
Vascular Graft	Common Iliac Bifurcation	Free Trapped Delivery System	Excessive Bleeding Requiring Transfusion	None	During the index procedure the left graft leg was extended to the external iliac to exclude a common iliac aneurysm. On withdrawal, the tip of the delivery system became trapped within the graft at the origin of the external iliac artery. A laparotomy was performed to retrieve the delivery system and renew the distal anastomosis.	Extension of graft to undersized external iliac
Adjunctive Stenting at Index						
Self-Expanding Stent	External Iliac Artery	Dissection	None	Excessive Bleeding Requiring Transfusion	During the index procedure a stent was placed in the left external iliac to treat dissection.	

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Adjunctive Endarterectomy at Index						
None	Femoral Artery	Stenosis of Native Vessel	None	Excessive Bleeding Requiring Transfusion	During the index procedure a right common femoral endarterectomy with pericardial patch angioplasty was performed for a large posterior plaque.	Access vessel
Open Conversion Performed at Index Procedure						
Adjunctive Revision to Open AAA Repair						
Vascular Graft	Aorta and Iliac Arteries	Separation of Endo-Conduit	Excessive Bleeding Requiring Transfusion	Graft Thrombosis	During the index procedure the subject had a very narrow ipsilateral access route that was treated with an endoconduit terminating in the common iliac artery. After placement of the primary graft, withdrawal of the delivery system detached the endoconduit from the common iliac artery causing substantial hemorhage. Bleeding was controlled by open surgery and open repair of the AAA. The patient died 4 days post-operatively from multi-organ failure.	Intra-op Conversion▲
Vascular Graft	Aorta and Iliac Arteries	Unsuccessful Gate exclusion Ilpositioned AUI Converter	None	Pulmonary Failure Requiring Intubation	At index procedure the primary graft was landed low in the aortic neck. Contralateral wire access was unsuccessful because of access vessel disection. An AUI converter was placed high in the aorta to overcome the poor placement of the primary graft. The converter did not connect with the ipsilateral limb of the graft and leakage into the sac persisted. The cause of leakage was not identified and the graft was removed and the AAA treated by open surgery. The patient had inoperable wide spread metastatic bladder cancer. He had undergone bladder resection and adjunctive chemotherapy prior to his AAA repair. One month prior to death he presented for weight loss. He became cachexic and then septic, and had hepatic failure with hepatic encephalopathy. On final admission he was DNR on palliative care with morphine.	Ilpositioned AUI converter. Intra-op Conversion▲
Vascular Graft	Aorta and Iliac Arteries	Access Failure	Excessive Bleeding Requiring Transfusion	None	During the index procedure in a very tortuous aorta, gate cannulation could not be achieved because of flattening of the gate. The right hypogastric artery had been inadvertently covered by the distal end of the graft and the repair was then successfully converted to open.	Intra-op Conversion▲
Adjunctive Treatment of Other Complications						
Addjunctive Extension of Stent Graft at Index						
Stent Graft	Common Iliac	Type Ib Endoleak	None	None	During the index procedure, an unplanned right distal extension was used with additional balloon angioplasty.	

Accessory Device	Affected Site	Reason for Implantation	Explicitly Related MAE	Other MAE	Narrative	Comment
Stent Graft	Aortic Neck	Type Ia Endoleak	None	None	During the index procedure a Type Ia endoleak was treated with a competitor proximal cuff	Competitor component used
Adjunctive Fem-Fem bypass at Index						
Vascular Graft	Common Iliac	Cannulation Failure and AUI Conversion	Excessive Bleeding Requiring Transfusion	None	At index procedure, ipsilateral limb was landed in the sac. Inaccurate crossover cannulation of gate resulted in guide wire returning down ipsilateral limb but was snared from contralateral side. Contralateral limb was landed within ipsilateral limb in error and AUI converter used.	Unplanned AUI
Adjunctive Stenting of Graft at Index Procedure						
Stent Graft	Distal Aorta	Type III Endoleak	None	None	During the index procedure a competitor proximal cuff was placed successfully to reline part of the stent graft.	Possible association with hyper-heparinization
Adjunctive Stenting of SMA						
Balloon-Expandable Stent	SMA	SMA Part Covered by Graft	Excessive Bleeding Requiring Transfusion	Excessive Bleeding Requiring Transfusion	During the index procedure, the anterior peak of the fishmouth of the graft inadvertently encroached on the SMA which was stent prophylactically.	

▲Indicates a case that did not receive an Aorfix™ implant at the end of the index procedure.

3.5 Patency, Conversion and Rupture:

Graft Patency at 12 months

Note that 1 subject was found post-operatively to suffer from a hypercoagulable condition. His endograft occluded completely two weeks post-operatively and an emergently placed axillo-bi-femoral graft also occluded after a similar period before the condition was diagnosed.

As listed above, 7 secondary procedures and 1 adjunctive procedure were performed to address stent graft leg patency. Particular causes of leg occlusion were:

- Distal extenders where the proximal end was incompletely dilated;
- Flow dividers that were located in a narrow aorta so that the contralateral gate compressed the attached ipsilateral limb; and
- Extreme oversizing of implants.

Renal stenoses and occlusions

As listed above, 6 secondary procedures and 3 adjunctive procedures were performed to address renal artery patency. Placement of proximal cuffs or balloon expandable stents is associated with more than half of all renal interventions.

Conversions

The majority of this section addresses the As Treated population (N=210). All but 1 conversion was performed during the index procedure in this study and so the following discussion of conversions addresses the Intention To Treat population so as to include all cases.

Of the 218 subjects enrolled in the study, 3 subjects were converted to an open surgical repair during the attempted Aorfix™ procedure. The first subject suffered a detachment of an endovascularly placed access conduit at the iliac artery on removal of the delivery system. A conversion was performed to control blood loss. The second subject was converted to an open procedure due to failure to cannulate the gate and a covered left hypogastric artery. Access could not be gained on the contralateral side in the third subject because of a dissection. For the third subject an incorrectly proximally placed AUI converter did not connect with the ipsilateral leg causing a persistent endoleak whose origin was incorrectly identified. A conversion was eventually performed to control the leak.

Of the 210 subjects who were successfully treated with an Aorfix™ graft, 1 subject (0.5%) was converted to an open procedure 30 days after the initial procedure secondary to a hypercoagulable state diagnosed post occlusion of the Aorfix™ endograft and the subsequently placed axillar bi-femoral graft.

Aneurysm Rupture

One (1) subject (0.5%) experienced a contained rupture at the sixth postoperative week. After extensive diagnostic radiology, it was concluded that no endoleak was present and the subject was managed conservatively. Review of device sizing indicates that the proximal diameter of the graft was undersized and the aortic neck showed high levels of thrombus pre-operatively. Over the first 12 months, the sac shrank 7% in volume but the

aortic neck dilated. The implant migrated slowly and a large size proximal cuff was fitted during the 13th postoperative month.

4. Sub-Group Analysis: Gender

Women are significantly less likely to meet device IFU criteria for endovascular aneurysm repair due to neck length, diameter, and angulation differences between genders[1]. Given the study's focus on highly angulated necks, a larger percentage of female subjects (28.9%, 63/218) were recruited. Therefore, additional sensitivity analyses can be performed on the effect of gender on the study's outcomes. Specifically, the effect of gender on: successful device deployment, adjunctive and secondary procedures, MAEs through 30 days and the composite effectiveness endpoint at 12 months were detailed below.

Device Deployment

Of the 8 subjects who did not successfully receive an Aorfix implant at their index procedure, 75% (6/8) were female.

Table 50 Reasons for not Receiving an Implant by Gender

	Male	Female
Narrow Access Vessel	0	50.0% (4/8)
Tortuous Access Vessel	12.5% (1/8)	0
Intra-operative Conversion	12.5% (1/8)	25% (2/8)

Adjunctive and Secondary Procedures

Table 51 lists adjunctive and secondary procedures by gender and type. Adjunctive procedures were approximately 50% more common in female patients and procedure-related secondary procedures were markedly elevated in female subjects, in both instances as a consequence of access challenges. As anticipated, there was no effect of gender seen on device-related secondary procedures.

[1] See Sweet, M et al

Table 51 Breakdown of Adjunctive and Secondary Procedures by Gender and Type

	Aorfix™ ITT Adjunctive Procedures		Aorfix™ As Treated Device-Related Secondary Procedures		Aorfix™ As Treated Procedure-Related Secondary Procedures	
Procedure	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
All Procedures	8.4% (13/155)	12.7% (8/63)	8.5% (13/153)	8.8% (5/57)	3.3% (5/153)	15.8% (9/57)
Graft leg loss of patency	0.6% (1/155)	0	3.3% (5/153)	1.8% (1/57)	0.7% (1/153)	0
Renal artery loss of patency	1.9% (3/155)	0	2.0% (3/153)	3.5% (2/57)	0	1.8% (1/57)
Type II Endoleak	0.6% (1/155)	0	0	0	2.0% (3/153)	3.5% (2/57▲)
Access Complication	1.9% (3/155)	7.9% (5/63)	0	0	0	7.0% (4/57▲)
Open Conversion at Index Procedure	0.6% (1/155)	3.2% (2/63)	0	0	0	0
Other Complication	2.6% (4/155)	1.6% (1/63)	3.3% (5/153)	3.5% (2/57)	0.7% (1/153)	3.5% (2/57)

▲Two events recorded for the same patient

Major Adverse Events at 30 Days

A similar effect is seen in the incidence of MAEs at 30 days (Table 52) with male subjects having an MAE rate of 22% and female subjects a rate of 30%. Substantially elevated rates of blood loss and surgical wound complication were seen in female patients.

Table 52 Effect of Gender on MAEs through 30 days

% (n/N) MAE through 30 days	Aorfix™ ITT Male N=155	Aorfix™ ITT Female N=63
Any Major Adverse Event	21.9% (34/155)	30.2% (19/63)

Effectiveness

Considering primary effectiveness (post-hoc analysis), 94% of male subjects were free from endoleak, migration or fracture whereas only 81% of female patients achieved the same result (Table 53).

Table 53 Effect of gender on primary effectiveness at 12 Months

% (n/N) Effectiveness Endpoint	Aorfix™ ITT Male N=155	Aorfix™ ITT Female N=63
All Aorfix™ Subjects Meeting Primary Effectiveness Endpoint	94.2% (97/103)	81.1% (30/37)
Number Aorfix™ with Type I or III Endoleak	0.9% (1/110)	2.5% (1/40)
Number Aorfix™ with Migration	0%	4.4% (2/45)
Number Aorfix™ with Fracture in sealing zone	5.0% (6/119)	9.5% (4/42)

These observations reflect the findings in the literature showing that female patients tend to have more complications and poorer outcomes with endovascular abdominal aortic surgery as compared to male patients.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

Comprehensive preclinical bench testing was performed on the Aorfix™ AAA Flexible Stent Graft System in accordance with US and international standards and guidance documents. The testing demonstrated that the Aorfix™ AAA Flexible Stent Graft System met the respective performance and design specifications. Preclinical *in-vivo* animal testing was conducted in order to evaluate acute and medium-term performance of the implant. Specifically, the study was performed to evaluate technical success, device integrity and histopathologic response for up to 26 weeks. The results support the safety and expected clinical performance of the Aorfix™ AAA Flexible Stent Graft System. Biocompatibility testing was conducted on the Aorfix™ AAA Flexible Stent Graft System to ensure that the finished device is biocompatible. All testing performed met the requirements as specified within the applicable standard. Laboratory testing demonstrated the strength, durability and utility of the Aorfix™ AAA Flexible Stent Graft System which met the requirements of the applicable standards.

The Aorfix™ AAA Flexible Stent Graft System is a single-use device that is provided sterile to the end user. The Aorfix™ AAA Flexible Stent Graft System is sterilized using

ETO sterilization and is validated to demonstrate a Sterility Assurance Level (SAL) of 10^{-6}.

A. Effectiveness Conclusions

210/218 subjects were implanted with the Aorfix™ AAA Flexible Stent Graft System. At the 12 month follow-up interval, 196 subjects were eligible for clinical and imaging follow-up, with 140 subjects having adequate data at this or a later follow-up interval to allow for an assessment of the post hoc primary effectiveness endpoint.

The composite effectiveness endpoint, that is, freedom from Type I and Type III endoleaks, migration >10mm and fracture in the fixation zone at one year, was 127/140 (90.7%) for the Aorfix study subjects with all neck angles, 37/40 (92.5%) with neck angles <60°, 67/75 (89.3%) with neck angles between 60° to 90°, and 90/100 (90%) with neck angles ≥ 60°. Of all subjects at 1 year, 1.2% showed aneurysm diameter expansion and 41.9% showed a decrease in aneurysm diameter, with no significant variation with neck angle. Two cases of migration were seen with the Aorfix™ AAA Flexible Stent Graft System. There was one Type I and one Type III endoleak reported at 1 year. Six percent (6%) of all subjects experienced a hook fracture and 2% had a fracture in the main body of the stent graft distal to the sealing zone. Subsequent to a material change, no further fractures have been seen.

A tipping point analysis suggested that the missing data does not bias the effectiveness conclusions for this study.

There were 3 intra-operative conversions and one late conversion. The late conversion was in a subject who received a conversion to open repair 2 weeks post- endovascular repair and was subsequently diagnosed with a hypercoaguable state which was medically managed after occlusion of the open graft. There was one post-operative contained aneurysm rupture. The subject continues to be followed, has had a proximal cuff placed secondary to migration that was seen post rupture, and has significant sac regression.

Re-interventions were most frequently performed to treat Type II endoleaks, stenosis or thrombosis of limbs and to treat access vessel disease and stenosed, compromised or occluded renal arteries. Compromised flow in limbs was associated with distal extension pieces that were too large for the target vessel or which had not been adequately dilated during implantation. Renal stenting occurred as an acute consequence of aggressive proximal placement of the graft. There have been no late renal stent events in this study.

Despite the limitations with the conduct of this clinical study, the information provided is adequate to provide a reasonable assurance of the effectiveness of the Aorfix™ AAA Flexible Stent Graft System for the treatment of abdominal and aorto-iliac aneurysms with necks up to 90°.

B. Safety Conclusions

Baseline medical history and anatomy were similar between the Aorfix™ and control group apart from the greater age, higher aortic neck angles and larger numbers of female subjects in the Aorfix™ group.

The post-hoc safety analysis, that is, freedom from MAEs within 30 days, was 76% (165/218) for the Aorfix™ ITT group and 59% (45/76) for the COS ITT group. All subjects were evaluable within 30 days of the procedure.

C. Risk Benefit Conclusions

As stated above, the outcomes for this study provide a reasonable assurance of the safety and effectiveness of the Aorfix™ AAA Flexible Stent Graft System for the specified intended use. For the patient, this means that they will likely not experience a major adverse event in the first 30 days after receiving this device and that their aneurysm will likely remain excluded from blood flow and pressure such that it will not rupture and cause death. This is particularly important for patients with aortic neck angles of greater than 60°, as there are no other endovascular grafts approved for treating this population and the alternative of open surgical repair is technically challenging and associated with relatively high morbidity.

The benefits of this treatment are likely to extend beyond 12 months.

In conclusion, the data provided in this PMA application demonstrate that the probable benefits of the Aorfix™ AAA Flexible Stent Graft System outweigh the probable risks for the endovascular treatment of abdominal and aorto-iliac aneurysms. Additional information will be provided from a post-approval study.

D. Overall Conclusions

The clinical study was performed in a uniquely challenging subject population in which approximately 70% had aortic neck angulations greater than 60° and more than 28% of subjects were female. Outcomes of abdominal surgery, both open and endovascular aneurysm repair, are widely reported to have higher rates of complication in females than the same surgery performed in males. The study has highlighted that female patients with AAA are more likely to have a neck angle greater than 60° than a less angled neck. The ability to treat such high neck angulation services the currently unmet need of all patients with neck angles greater than 60° and is of particular value to female patients with aortic aneurysms.

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. As expected, there were slightly higher rates of adverse events in subjects with highly angled aortic necks. The risks associated with these events can be diminished with adequate subject selection and follow-up.

XIII. CDRH DECISION

CDRH issued an approval order on February 14, 2013 The final conditions of approval cited in the approval order are described below.

The applicant has agreed to provide the following data as part of the Annual Report to your PMA application:

1. They will provide a clinical update to physician users at least annually. At a minimum, this update will include, for your long-term post-approval study cohort, a summary of the number of patients for whom data are available, with the rates of aneurysm-related mortality, aneurysm rupture, secondary endovascular procedures, conversion to surgical repair, complications, endoleak, aneurysm enlargement, prosthesis migration, and patency. 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 is 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 the Annual Report.

   In addition to the Annual Report requirements outlined above, the applicant agrees to conduct a post-approval study to evaluate freedom from aneurysm-related mortality (ARM) through 5 years post-implantation in a cohort consisting of newly enrolled patients plus continued follow-up of patients from the premarket clinical study, as described below, and to provide the data from this study in separate post-approval study reports.

2. The long-term follow-up study will be a prospective, consecutively enrolling, single-arm, multicenter study that will consist of continued follow-up of all available subjects from the pivotal study and the continued access study, as well as newly enrolled (*de novo*) subjects from this PAS. A total of 455 subjects will be enrolled, with at least 282 evaluable at five years post-implantation. A minimum of 234 subjects will be newly enrolled at a minimum of 20 investigational sites across the United States.

   The primary safety endpoint of the study is freedom from aneurysm-related mortality at five years post-implantation, which will be compared to a performance criterion of 94%. Aneurysm-related mortality is defined as:

   > *Death from any cause within 30 days of the primary repair of the aneurysm, or any associated secondary procedure or surgical conversion, or any death due to aneurysm rupture or related to the aneurysm repair or device complications. Any death occurring within 30 days of any procedure used to treat the aneurysm will be considered due to the procedure, unless clear evidence (i.e. a death certificate) exists to the contrary.*

   Secondary endpoints through five years will include all major adverse events (MAE) as defined in your protocol and serious adverse events (SAE), including aneurysm rupture, conversion to open surgical repair, endoleak, fracture in the fixation zone, migration, expansion of the aneurysm sac, and graft patency.

3. The applicant has agreed to implement a training program, as outlined in your PAS protocol. Your post-approval study reports to your PMA will include a subset analysis examining the skills of new practitioners in the use of the Aorfix Flexible Stent Graft System. All centers will take part in the SVS Vascular Quality Initiative (VQI) which will allow the centers to compare their outcomes with regional and national outcomes. The statistical data from VQI will be used to identify training shortfalls and opportunities to improve outcomes. Should modifications be necessary to the training program, you will describe and justify each modification within the post-approval study reports. Additionally, if any insights are obtained regarding your training program, you will provide a discussion of that in the post-approval study report. Please be advised that the results from these studies should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

   The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

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

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

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