SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Endovascular Graft

Device Trade Name: Alto™ Abdominal Stent Graft System

Device Procode: MIH

Applicant's Name and Address: Endologix, Inc.
3910 Brickway Blvd.
Santa Rosa, CA 95403

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P120006/S031

Date of FDA Notice of Approval: March 13, 2020

The Alto™ Abdominal Stent Graft System is Endologix's next generation polymer-based abdominal stent graft system, based on the Ovation Abdominal Stent Graft System.

The original PMA (P120006) for the Ovation Abdominal Stent Graft System was approved on October 5, 2012 and is indicated for treatment of patients with abdominal aortic aneurysms having vascular morphology suitable for endovascular repair. Changes to the Ovation delivery system were made to enhance ease of use during deployment via a PMA real-time supplement (i.e., P120006/S001, approved December 11, 2012) and marketed under the Ovation Prime Abdominal Stent Graft System trade name. Additional changes to the Ovation Prime delivery system were made via a PMA real-time supplement (i.e., P120006/S020, approved on July 17, 2015) and marketed under the Ovation iX™ Abdominal Stent Graft System trade name. The Summary of Safety and Effectiveness Data (SSED) to support the Ovation Abdominal Stent Graft System is available on the CDRH website and is incorporated by reference here.

Ovation Abdominal Stent Graft System (Original PMA Approval):
https://www.accessdata.fda.gov/cdrh_docs/pdf12/p120006b.pdf

This Panel Track PMA Supplement was submitted to obtain approval for the Alto™ Abdominal Stent Graft System, a modified device design from the Ovation iX™ Abdominal Stent Graft System, for the treatment of patients with infrarenal abdominal aortic aneurysms having the appropriate anatomy.

II. INDICATIONS FOR USE

The Alto™ Abdominal Stent Graft System is indicated for treatment of patients with infrarenal abdominal aortic aneurysms having the vascular morphology suitable for endovascular repair with the device, which includes the following:

- Adequate iliac/femoral access compatible with vascular access techniques (femoral cutdown or percutaneous), devices, and/or accessories,
- A proximal aortic landing zone for the sealing ring 7mm below the inferior renal artery.
- An aortic sealing zone comprised of healthy aorta defined as:
    - Lack of significant thrombus > 8 mm in thickness; at any point along the aortic circumference at the level of 7mm below the inferior renal artery,
    - Lack of significant calcification at the level of 7mm below the inferior renal artery,
    - Conicity < 10% as measured from the inferior renal artery to the aorta 7mm below the inferior renal artery,
    - An inner wall diameter of no less than 16 mm and no greater than 30 mm at 7 mm below the inferior renal artery, and
    - An aortic angle of ≤ 60 degrees.
- A distal iliac landing zone:
    - With a length of at least 10 mm, and
    - With an inner wall diameter of no less than 8 mm and no greater than 25 mm.

III. CONTRAINDICATIONS

- Patients who have a condition that threatens to infect the graft.
- Patients with known sensitivities or allergies to the device materials including polytetrafluoroethylene (PTFE), polyethylene glycol (PEG)-based polymers, contrast agents, fluorinated ethylene propylene (FEP), titanium, nickel, platinum, or iridium.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Alto™ Abdominal Stent Graft System Instructions for Use.

V. DEVICE DESCRIPTION

The Alto™ Abdominal Stent Graft System is an endovascular device delivered via a low-profile catheter to treat abdominal aortic aneurysms (AAAs). The stent graft is designed to reline the diseased vasculature, providing an endovascular blood conduit for isolating the aneurysm from the high-pressure flow of blood, thereby reducing the risk of rupture. The

stent graft is a modular configuration comprised of an aortic body section, iliac limbs, and iliac extensions as required (**Figure 1**).

The Alto™ Abdominal Stent Graft System includes:

- An Aortic Body Stent Graft and delivery catheter
- Ovation iX™ Iliac Limb Stent Grafts and delivery catheters
- Ovation iX™ Iliac Extension Stent Grafts and delivery catheters (as required)
- CustomSeal™ Polymer Fill Kit
- Autoinjector 2

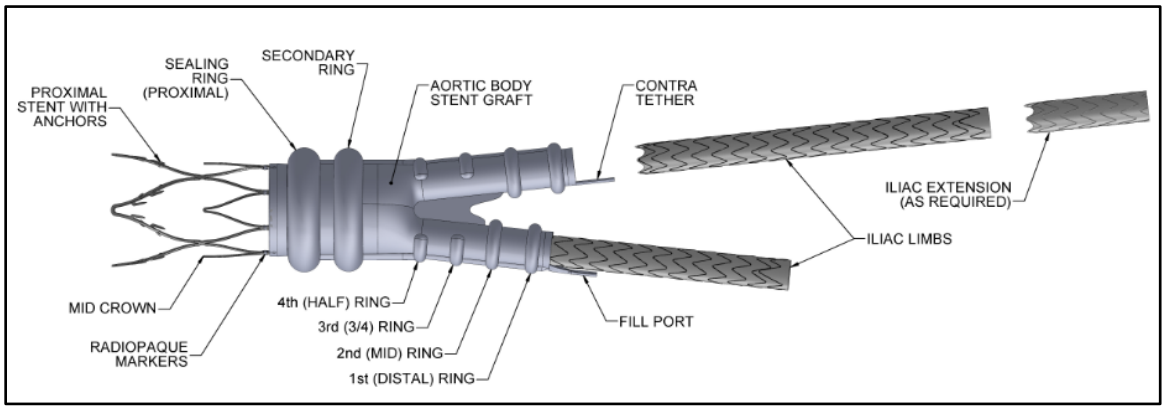


Figure 1: Schematic of Alto™ Abdominal Stent Graft System

The Alto™ Abdominal Stent Graft System incorporates the following primary modifications to the currently approved Ovation iX™ Abdominal Stent Graft System:

- Locating Sealing Ring 7mm below renal arteries,
- Inclusion of webbing between the aortic body legs at the graft bifurcation,
- Standardization of the aortic body leg diameter,
- Lengthened contralateral leg,
- Graft laminate layer composed of fewer discrete PTFE pieces and one additional wrapped PTFE layer,
- Incorporation of an integrated balloon into the delivery system, and
- Use of a lower pressure Autoinjector 2.

The Alto™ Abdominal Stent Graft System includes a modified location of the sealing ring, with the center of the sealing ring being nominally 7mm below the graft edge and corresponding to the location of the proximal aortic landing zone where the aortic artery is 16 – 30mm in diameter. The Alto™ Abdominal Stent Graft System was also modified to include webbing between the aortic body legs at the graft bifurcation to improve leg stability during cannulation. Additionally, the Alto™ Abdominal Stent Graft System was modified to have a standardized aortic body leg diameter of 11 mm to improve ease of cannulation, a lengthened contralateral leg to enhance differentiation of the contralateral

and ipsilateral legs under fluoroscopy, and a graft laminate layer composed of fewer discrete PTFE pieces and one additional wrapped PTFE layer as compared to the previously approved Ovation Abdominal Stent Graft Systems. Additionally, the Alto™ Abdominal Stent Graft Delivery System incorporates use of an integrated balloon to ease deployment and uses a lower pressure Autoinjector 2 to inject the fill polymer.

Aortic Body

The aortic body is comprised of a proximal stent for suprarenal fixation and a low-permeability polytetrafluoroethylene (PTFE) graft connected using discrete attachments and attachment coils as shown in **Figure 2**. The bare proximal stent is designed with 8 anchors to help fixate the device to the aortic wall. For delivery, the stent is in a compressed state within the catheter. When released from the compressed state, the stent expands to engage the vessel wall.

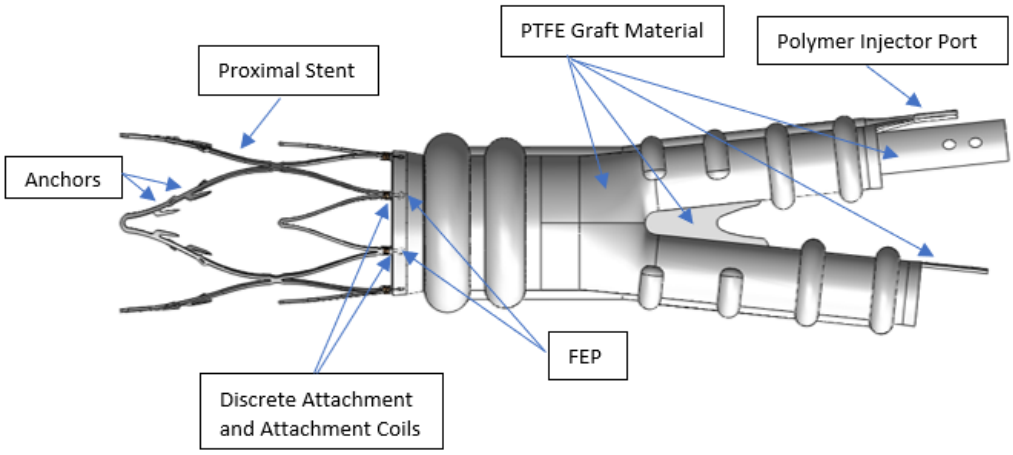


Figure 2: Image of Alto™ Aortic Body Stent Graft

Please reference the Alto™ Aortic Body Stent Graft Materials below in **Table 1**.

Table 1: Aortic Body Stent Graft Materials

Implant Component	**Material**
Graft	Polytetrafluoroethylene (PTFE)
Polymer Injector Port	Polytetrafluoroethylene (PTFE)
Proximal Stent	Nickel-Titanium (Nitinol) Alloy
Discrete Attachments	Nickel-Titanium (Nitinol) Alloy with FEP
Radiopaque Markers (Attachment Coils)	Nickel-Titanium (Nitinol) Alloy

The nitinol proximal stent is radiopaque, and radiopaque markers (attachment coils) are located adjacent to the graft proximal edge. These radiopaque markers aid in the placement of the device in its intended location relative to the renal arteries. The fill polymer is radiopaque and provides visualization of the polymer fill channels once the graft is filled.

Iliac Limbs/Extensions

The iliac limbs and extensions are comprised of a nitinol stent encapsulated in low-permeability PTFE. The materials can be referenced in **Table 2** below. The iliac limbs are deployed into the leg sections of the aortic body. Radiopaque markers enable the physician to visualize the appropriate iliac limb - aortic body overlap or iliac extension – iliac limb overlap during a catheter-based deployment.

Table 2: Iliac Limb/ Extension Stent Graft Materials

Implant Component	**Material**
Graft	Polytetrafluoroethylene (PTFE)
Stent and Attachments	Nickel-Titanium (Nitinol) Alloy
Radiopaque Markers	Platinum-Iridium Alloy

Delivery System

To facilitate device introduction into the access vessel, the aortic body, the iliac limbs, and the iliac extensions are preloaded into delivery catheters as illustrated in **Figures 3 - 4**. The delivery catheters each have a lumen for use with a .035" (0.89 mm) guidewire to facilitate access and deployment. The outer sheaths are hydrophilic coated. There are two variations of the delivery system: one for the aortic body stent graft (**Figure 3**) and one for the iliac limbs/extensions (**Figure 4**). Both systems allow for the inner catheter to be withdrawn through the outer sheath, with the outer sheath and integrated hemostatic valve remaining in the vasculature to facilitate the introduction of ancillary devices.

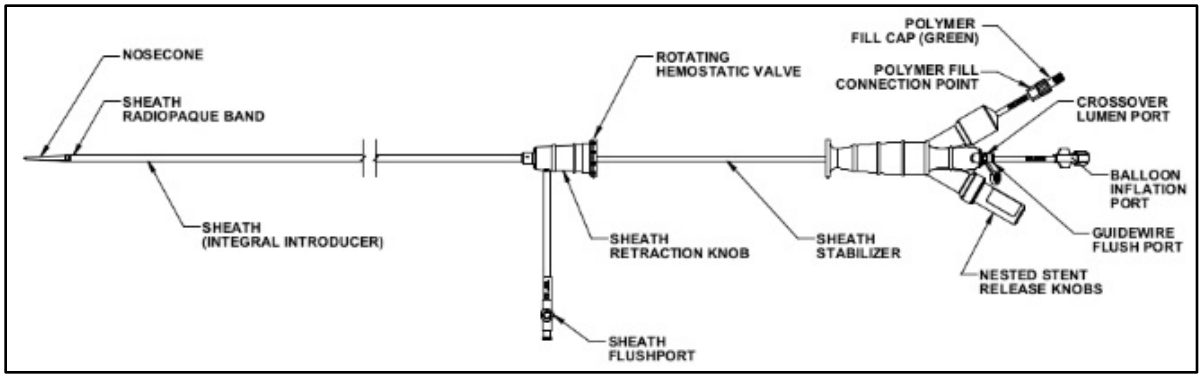


Figure 3: Schematic of Alto™ Abdominal Stent Graft System Aortic Body Delivery Catheter

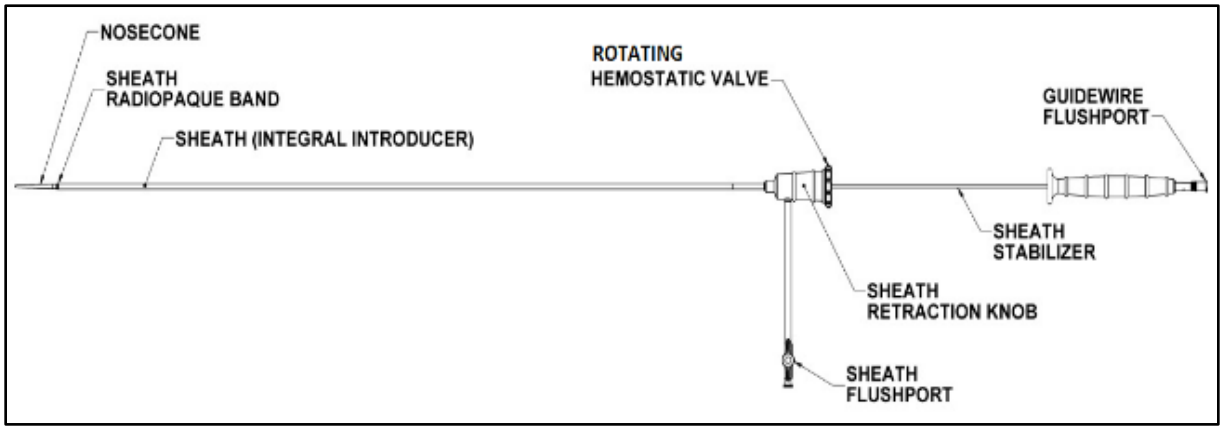


Figure 4: Schematic of Ovation iX™ Iliac Limb/ Iliac Extension Delivery Catheter

The aortic body is deployed via the aortic body delivery catheter (**Figure 3**), which has a working length of approximately 60cm and outer sheath diameter of 15Fr (inner diameter 13Fr). The catheter has a connection to the distal legs of the aortic body. During aortic body stent graft deployment, the device is first positioned, and the sheath is retracted. The proximal stent is deployed using stent release knobs on the handle, with an integral balloon used to facilitate graft opening. The fill polymer is then delivered through the fill connector port using the Autoinjector 2.

The contralateral and ipsilateral iliac limbs are each deployed via iliac limb delivery catheters (**Figure 4**). After deployment of the aortic body, a guidewire is placed from the contralateral access site into the contralateral distal leg of the aortic body; the integrated crossover lumen on the aortic body delivery system can be utilized to facilitate the process.

Please refer to the Alto™ Abdominal Stent Graft System Instructions for Use for additional description on the implants and associated delivery systems.

Alto™ Abdominal Stent Graft System Sizing

The Alto™ Abdominal Stent Graft System is designed to accommodate various aortic anatomies, including a range of proximal and distal aortic diameters, aneurysm lengths, and common iliac artery diameters. Refer to **Tables 3-5 below** for product sizes and configurations.

Table 3: Alto™ Aortic Body Stent Graft Sizes

Stent Graft Proximal Diameter, mm	Catheter Working Length, cm	Delivery System Outer Profile, F	Integral Sheath Inner Diameter, F	Covered Stent Graft Length, mm
20	60	15	13	80
23				
26				
29				
34				

Table 4: Ovation iX™ Iliac Limb Sizes

Stent Graft Proximal Diameter, mm	Stent Graft Distal Diameter, mm	Catheter Working Length, cm	Delivery System Outer Profile, F	Integral Sheath Inner Diameter, F	Covered Stent Graft Length, mm
14	10	60	12	10	80
	10				100
	10				120
	10				140
	10				160
	12				80
	12				100
	12				120
	12				140
	12				160
	14				80
	14				100
	14				120
	14				140
	14				160
	16		13	11	80
	16				100
	16				120
	16				140
	16				160
	18				80
	18				100

Stent Graft Proximal Diameter, mm	Stent Graft Distal Diameter, mm	Catheter Working Length, cm	Delivery System Outer Profile, F	Integral Sheath Inner Diameter, F	Covered Stent Graft Length, mm
	18				120
	18				140
	18				160
	22		14	12	80
	22				100
	22				120
	22				140
	22				160
	28		15	13	80
	28				100
	28				120
	28				140
	28				160

Table 5: Ovation iX™ Iliac Extension Sizes

Stent Graft Proximal & Distal Diameters, mm	Catheter Working Length, cm	Delivery System Outer Profile, F	Integral Sheath Inner Diameter, F	Covered Stent Graft Length, mm
10	60	12	10	45
12				
14				
16		13	11	
18				
22		14	12	
28		15	13	

Polymer Fill Kit (CustomSeal™ Kit) and Autoinjector 2

The CustomSeal™ Kit is comprised of two fill syringes containing fill polymer, which is used to inflate a network of channels and rings in the aortic body (refer to **Figure 1** above) and solidifies during the deployment procedure. The fill polymer is comprised of three components that are mixed within the fill syringes prior to injection into the aortic body stent graft. The components include a buffered solution containing a contrast agent which resides in one syringe and a reactive monomer that resides in the other syringe. The third

component is a separate reactive monomer that resides within the connecting tube between syringes. The reaction between the two monomers results in the formation of a solid hydrogel within the primary sealing ring, secondary support ring, fill channels, and leg support rings in the graft material of the aortic body (refer to **Figure 1**) during the deployment procedure. The CustomSeal™ Kit (**Figure 5**) is labeled with a 14 minute detach time, meaning the aortic body delivery catheter should not be disconnected from the graft until the polymer has had 14-minutes to cure.

Upon mixing and injection into the aortic body stent graft, the polymer components form a radiopaque cross-linked polymer that fills the primary sealing ring, fill channels, and support rings in the graft material of the trunk and legs of the aortic graft. The fill polymer radiopacity dissipates over time (1-2 months) so as not to create imaging artifacts that could interfere with endoleak detection in subsequent CT imaging follow-up.

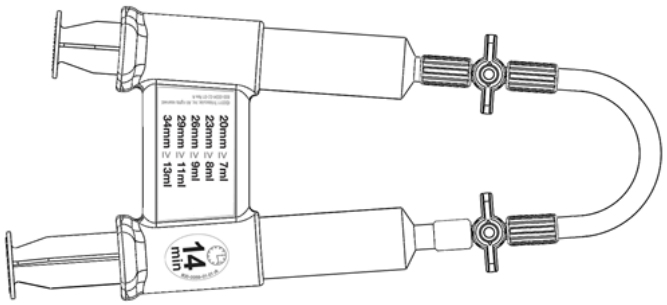


Figure 5: CustomSeal™ Kit with 14-minute Disconnection Time

Alto™ Abdominal Stent Graft System Specific Anatomic Considerations

The specific design features of this endovascular graft impact how to assess a patient's suitability for treatment. The following diagrams indicate the specific anatomic considerations that should be considered when evaluating suitability for treatment with the device as described in the Indications for Use statement.

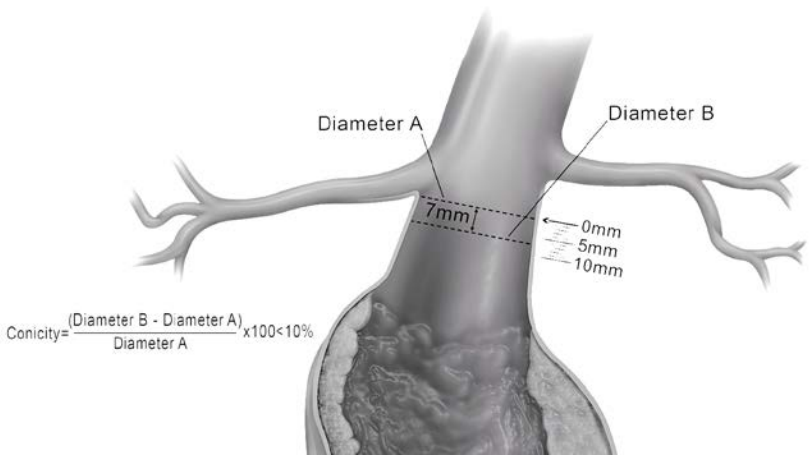


Figure A: Proximal Landing Zone and Conicity

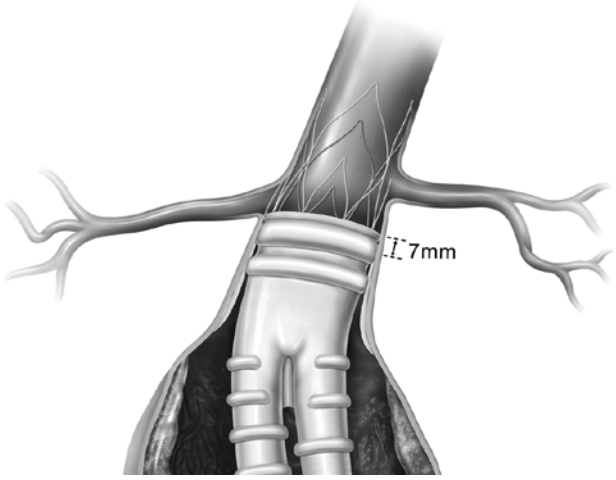


Figure B: Proximal Landing Zone

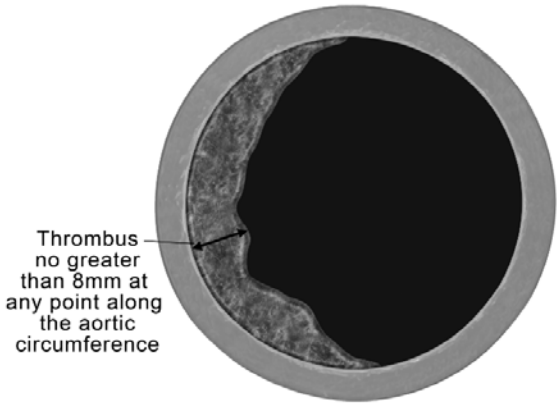


Figure C: Sealing Zone Thrombus

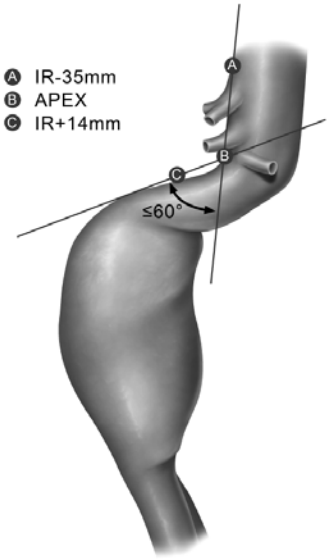


Figure D: Aortic Angle

VI. ALTERNATE PRACTICES AND PROCEDURES

There are several alternatives for the treatment of infrarenal abdominal aortic aneurysms, including medical management, open surgical repair, or endovascular repair using another endovascular graft system. 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 Alto™ Abdominal Stent Graft System has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

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

- Acute and chronic renal failure, renal microembolism, renal insufficiency, renal artery occlusion, contrast toxicity;
- Amputation;
- Anesthetic complications and subsequent attendant problems (aspiration);

- Aneurysm enlargement or rupture;
- Aortic damage (perforation, dissection, bleeding, rupture);
- Aortocaval fistulae;
- Aortoenteric fistulae;
- Blood or bleeding events such as anemia, gastrointestinal bleeding, retroperitoneal bleeding;
- Bowel events such as bowel ischemia, infarction, bowel necrosis, colon ischemia, paralytic or adynamic ileus, obstruction, fistula;
- Cardiac events and subsequent attendant problems such as congestive heart failure, volume overload, arrhythmias, myocardial infarction, chest discomfort or angina, elevations in creatinine phosphokinase (CPK), hypotension, hypertension;
- Cerebral events (local or systemic) and subsequent attendant problems such as change in mental status, cerebrovascular accident (hemorrhagic or embolic), reversible ischemic neurologic deficit, nerve injury, transient ischemic attacks, paraplegia, paraparesis, paralysis;
- Claudication;
- Contrast toxicity/anaphylaxis;
- Death;
- Device events such as deployment or device malfunction, stent fracture, loss of stent graft system component integrity, graft twisting and/or kinking, graft material wear, dilation, erosion, puncture, endograft occlusion, migration, dislodgement, endoleak;
- Edema;
- Embolic and thrombotic events (with transient or permanent ischemia or infarction) such as deep vein thrombosis, thromboembolism, microembolism, thrombophlebitis, phlebothrombosis, air embolism;
- Endoleaks (or perigraft flow);
- Fever;
- Gastrointestinal complications;
- General discomfort related to the procedure;
- Generalized inflammatory response that may be associated with elevated levels of systemic mediators of inflammation, elevated temperature;
- Genitourinary complications and subsequent attendant problems such as ischemia, erosion, fistula, incontinence, hematuria, infection;
- Hematoma (surgical);
- Hepatic failure;
- Hypersensitivity (severe allergic reaction and/or anaphylactoid response) to x–ray contrast dye, anti-platelet therapy, device materials including polytetrafluoroethylene (PTFE), polyethylene glycol (PEG)-based polymers, contrast agents, fluorinated ethylene propylene (FEP), titanium, nickel, platinum, or iridium;
- Insertion and other vascular access site complications such as infection, dissection, transient fever, bleeding, pain, delayed healing, abscess formation, hematoma, dehiscence, seroma, cellulitis, nerve injury/damage, neuropathy,

neuralgia, vasovagal response, pseudoaneurysm, anastomotic false aneurysm, arteriovenous fistula;
- Impotence/ sexual dysfunction;
- Improper stent graft placement;
- Incomplete stent graft deployment;
- Insertion and removal difficulties;
- Lymphatic complications and subsequent attendant problems such as lymphocele, lymph fistula;
- Multi-system organ failure;
- Neoplasm;
- Open surgical conversion;
- Operative and post–operative bleeding and hemorrhage, coagulopathy;
- Paralysis (temporary or permanent) such as paraplegia, monoplegia, paresis, spinal cord ischemia, hemiplegia, bowel or bladder incontinence;
- Pericarditis;
- Pneumothorax;
- Polymer leak with hypersensitivity reaction;
- Possible infection–urinary tract, systemic or localized (access site), endograft;
- Prosthesis occlusion/stenosis;
- Pseudoaneurysm;
- Pulmonary/respiratory events and subsequent attendant problems such as pulmonary insufficiency, pneumonia, respiratory depression or failure, pulmonary edema, pulmonary embolism, atelectasis, pleural effusion;
- Radiation injury, late malignancy;
- Renal failure/renal insufficiency
- Sepsis;
- Seroma;
- Shock;
- Spinal neurological deficit;
- Stenosis/occlusion of native vessel
- Surgical conversion to open repair; and/or
- Vascular spasm or vascular injury/trauma including damage to blood vessels and surrounding tissues, atherosclerotic ulcer, vessel dissection, perforation, plaque dissection, stenosis, pseudoaneurysm, vessel occlusion, embolization, ischemia, tissue loss, limb loss, gangrenous disease, worsened or new onset claudication, edema, fistula, bleeding, rupture, death.
- Wound or access site complications.

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

IX. SUMMARY OF NONCLINICAL STUDIES

The following non-clinical studies were performed on the Alto™ Abdominal Stent Graft System:

A. Laboratory Studies

Attributes, specifications and use conditions of the Alto™ Abdominal Stent Graft System were evaluated against bench testing previously submitted for the Ovation Abdominal Stent Graft System (P120006), the Ovation Prime Abdominal Stent Graft System (P120006/S001), the Ovation iX™ Iliac Stent Graft (P120006/S015) and the Ovation iX™ Abdominal Stent Graft System (P120006/S020).

Where applicable, additional testing was conducted to confirm the *in vitro* performance of the Alto™ Abdominal Stent Graft System. This testing focused on the aspects of performance that could have been impacted by the unique design characteristics of the device as compared to previous generations. It included bench testing to support compatibility and functionality of Autoinjector 2 with the Alto™ Abdominal Stent Graft System.

Bench testing was performed per Endologix's test protocols, which incorporated the requirements of ANSI/AAMI/ISO 25539-1:2003/Amendment 1:2015/(R)2009, Cardiovascular Implants – Endovascular Devices – Part 1: Endovascular Prostheses (equivalent to BS EN ISO 25539-1:2009) and Guidance for Industry and FDA Staff, *Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems – Guidance for Industry and FDA Staff* (April 18, 2010).

Testing was conducted on a subset of device configurations/sizes, or worst-case for each test, as appropriate, to represent the entire Alto™ Abdominal Stent Graft System range of sizes available. Test methods and results are summarized in **Table 6**, **Table 7** and **Table 8** and organized according to (1) System Level, (2) Delivery System, and (3) Stent Graft testing, respectively.

Bench testing is presented within the *in vitro* bench test results as part of **Table 6**.

All *in vitro* bench tests produced acceptable results.

The Alto™ Aortic Body Stent Graft System Level testing (with the Autoinjector 2) is provided in **Table 6** below.

Table 6: Alto™ Aortic Body Stent Graft System Level Testing

Test Name	Test Purpose	Acceptance Criteria	Results
Simulated Use	Design validation tests to evaluate device deliverability,	The delivery system shall deploy and fill the stent graft within the simulated use model without failure to: access, deploy the stents, fill the graft, enable contralateral wire access via the integral	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
	deployment, and removal.	crossover lumen, enable ballooning of the aortic body sealing rings [requirement unique to Alto™], disconnection between fill tube and the Alto™ aortic body, or withdraw the catheter. This device must be evaluated using an *in vitro* approximation of the clinical setting for the device.	
Product Performance, Post Sterilization	To confirm the Alto™ stent graft system can withstand two EtO sterilization cycles without compromising performance as evaluated in simulated use.	The stent graft systems must withstand two EtO sterilization cycles without compromising performance as evaluated in simulated use. The autoinjector must withstand e-beam sterilization without compromising performance as evaluated in simulated use.	Pass

The Alto™ Aortic Body Stent Graft Delivery System testing is provided in **Table 7** below.

Table 7: Alto™ Aortic Body Stent Graft Delivery System Testing

Test Name	Test Purpose	Acceptance Criteria	Results
Delivery System Placement Accuracy	To provide assurance of the ability to successfully place the stent graft in the *in vivo* environment.	The system must permit consistent and accurate deployment of the aortic body implant to within +5/-0 of the intended proximal aortic landing site. The sign convention: minus = toward heart, plus = away from heart. The system must permit consistent and accurate deployment of the implant to within ±5mm of the distal iliac landing site.	Pass
Delivery System Hemostasis	To confirm the ability of the device to maintain adequate hemostatic seal.	The hemostatic seals on the catheter shall not leak water at a rate greater than 7 ml/min under simulated use conditions. a) The maximum allowable delivery system leak rate (sheath seal, proximal handle assembly and guidewire lumen) is 7 ml/min for water under simulated use conditions. b) The maximum allowable introducer sheath (integral sheath seal) leak rate is 7 ml/min for water under simulated use conditions.	Pass
Delivery System Radiopacity	To ensure adequate visibility of the delivery system required for completion of the procedure.	The delivery system must have sufficient radiopacity as rated during simulated use and/or animal deployments under fluoroscopy to orient the implant, to confirm sheath retraction, to confirm fill tube disconnection between the Alto™ aortic body, to position the integral balloon, and confirm catheter withdrawal from the implant.	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
Delivery System Unsheathing Force	To determine the force to deploy the prosthesis under simulated anatomical conditions.	The unsheathing force shall not exceed the minimum tensile strength of the sheath tubing and shall not exceed an ergonomic limit of 12 lbs.	Pass
Delivery System Kink Resistance	Design validation test to ensure the device does not kink during simulated clinical use.	The catheter can be advanced through the tortuous flow model and does not kink in a way that compromises the deployment or damages the implant.	Pass
Delivery System Kink Resistance (Worst Case)	To evaluate the limits of kink resistance of the device in a bench-top model.	The catheter can resist kinking in mechanically simulated worst case clinical conditions (i.e. radius of curvature). Catheters which kink must successfully advance through the tortuous flow model, deliver the device, and be withdrawn.	Pass
Delivery System Length	To determine the working length of the delivery system.	The delivery system should provide an insertion length of 58 to 62 cm.	Pass
Delivery System Pushability	Design validation test to ensure the device provides adequate force transmission to allow for proper positioning.	The delivery system must transmit sufficient pushability to position the catheter at the correct elevation within the simulated use model for an accurate placement of the stent graft.	Pass
Delivery System Profile	To determine the profile of the delivery system.	The delivery system outer diameter (OD) must not exceed 15.4F for the largest aortic body.	Pass
Delivery System Bond Strengths	To confirm adequate tensile bond strength of the delivery system to permit access, deployment, and withdrawal from the vasculature.	<u>Minimum Tensile Strength:</u> Crown Support to Guidewire Lumen, Polymer Fill Tube Fitting to handle assembly, Balloon Fill Tube Fitting to handle assembly, Flushport Fitting to Flushport to Flushport body: 10 lbf	Pass
Delivery System Autoinjector 2 Pressure Range	To ensure adequate pressure is applied by the Autoinjector to fill the stent graft with polymer while not exceeding the burst pressure of the graft.	Must supply a pressure of 10.0 – 14.9 psi 30 seconds after insertion of syringe into autoinjector.	Pass
Delivery System Trackability	Design validation test to ensure the device can sufficiently track over a guidewire to the intended deployment location in a simulated use environment.	The delivery system must have sufficient trackability to position the catheter and accurately position the implant within the simulated use model.	Pass
Delivery System Torquability	Design validation test to ensure the delivery system provides adequate torque transmission to position and orient the device in a simulated use environment.	The Aortic Body delivery system must have sufficient torquability to position the catheter and accurately position and orient the implant within the simulated use model. When placed in simulated tortuous anatomy, the tip of the sheathed catheter must rotate 180° +/- 60°	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
		after a maximum rotation lag of 90° when the handle and flushport are rotated 180°.	
Torque Strength	To confirm adequate torsional bond strength of the delivery system during delivery, deployment, and withdrawal from the vasculature.	Each device must complete rotational conditioning without a failure that compromises the ability to place and deploy the implant and withdraw the delivery catheter. The safety factor for number of rotations shall be ≥ 1 for each test sample.	Pass
Delivery System Graft Retention	To ensure the graft does not prematurely detach from the delivery system during normal use of the device.	The system must not allow the delivery system fill tube to disconnect from the aortic body graft at a force less than 2 lbs prior to releasing the retention fitting. The Contralateral Leg Retention Tab on the Alto™ aortic body stent graft must remain intact and attached to the delivery catheter during deployment in simulated tortuous anatomy.	Pass
Delivery System Crossover Lumen Strength	To confirm adequate tensile bond strength of the crossover lumen tube to the lumen spacer junction.	The tensile strength of the crossover lumen/lumen spacer junction must exceed 1.5 lbf. The crossover lumen retention must remain intact during deployment in simulated tortuous anatomy.	Pass
Delivery System De-Mate	To ensure the detachment and withdrawal of the delivery system does not significantly affect the integrity of the implant.	The system must permit consistent withdrawal of the delivery system without causing damage to or more than 5mm dislodgement of the implant.	Pass
Delivery System Sheath Insertion Force	To confirm adequate lubricity due to coating on the delivery system for the Ovation iX™ limb.	Maximum sheath insertion force must be less than 1.0 lbf.	Pass
Integral Balloon Inflation Time	To characterize the time required to expand the integrated balloon in the delivery system, to the maximum recommended inflation volume.	The time required to expand the balloon to the maximum recommended inflation volume will be characterized.	Characterization only
Integral Balloon Deflation Time	To confirm the time required to deflate the integrated balloon in the delivery system from the maximum recommended inflation volume.	The system must be able to be repositioned within 30 seconds of the start of deflation.	Pass
Integral Balloon Fatigue	To ensure the balloon may be inflated an adequate number of cycles without loss of function.	The balloon must withstand 10 inflation / deflation cycles to the maximum recommended inflation volume without loss of integrity.	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
Integral Balloon Diameter by Volume	To confirm balloon diameter is large enough to enable primary sealing ring apposition within the vessel wall.	The balloon diameter versus inflation volume will be characterized. The balloon diameter must meet or exceed graft bore diameter within the range of inflation volumes characterized. Balloon diameter must be large enough to enable improvement in the primary sealing ring apposition with the vessel wall.	Pass
Integral Balloon Burst Strength	To confirm adequate burst strength of the balloon.	The balloon burst volume must exceed the recommended inflation volume.	Pass
Balloon Bond Tensile Strength	To confirm adequate tensile bond strength of the balloon bonds .	The tensile strength of the balloon bonds must exceed 3.4 lbf.	Pass
Catheter Guidewire Compatibility	To confirm the device can track over a commonly available guidewire size in order to aid in advancing the device to the treatment site.	The guidewire lumen must accept a 0.035" guidewire with little or no resistance.	Pass
Catheter Luer Compatibility	To confirm the catheter is compatible with ANSI ISO luer fittings in order to interface with other accessories.	The catheter must be compatible with ANSI ISO luer fittings.	Pass
Introducer System Compatibility	To confirm the delivery system can fit through commercially available introducers, when required.	Delivery system must fit through at least one commercially available introducer.	Pass
Crossover Lumen Guidewire Compatibility	To confirm a 0.018" guidewire can pass through the crossover lumen in order to facilitate cannulation.	The crossover lumen must accept a 0.018" guidewire.	Pass

The Alto™ Aortic Body Stent Graft testing is provided in **Table 8** below.

Table 8: Alto™ Aortic Body Stent Graft Testing

Test Name	Test Purpose	Acceptance Criteria	Results
Stent Graft Treatment Diameters	To confirm the stent graft can treat aortic lesions with luminal diameters within the device indications.	The implant must seal a mock aorta with luminal diameters ranging from 16mm to 30mm at the proximal sealing ring location.	Pass
Stent Graft Conformability to Vessel Wall	To confirm the stent graft will adequately seal in	Appropriately-sized aortic body grafts will seal in simulated 16 and 30 mm proximal vessels.	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
	vessel diameters within the device indications.	The stent graft should provide an effective treatment via sealing the aneurysm from blood pressure in diseased, non-uniform simulated vessels.	
Stent Graft Lumen Burst Strength	To confirm adequate burst strength of the stent graft lumen.	The aortic body graft must not burst below a pressure of 320 mmHg [6.2 psi] before or after dilatation to nominal balloon pressure with a balloon sized to the nominal graft ID.	Pass
Stent Graft Longitudinal Tensile Strength	To confirm adequate longitudinal tensile strength of the stent graft.	Must withstand the maximum forces exerted on the graft by either a transient systolic pressure of 320 mmHg or a pull force of 2.0 lbs. [the graft fill port safety specification]. For the 34mm size device, the 320mmHg minimum pressure load corresponds to a minimum tensile force of 7.0 lbs.	Pass
Stent Graft Length to Diameter Relationship (Characterization only)	To characterize the graft length to diameter relationship.	Any foreshortening (length to diameter relationship) of the aortic body during deployment must be characterized.	Characterization Only
10-yr Device Integrity – Graft Stent Attachment Creep	To evaluate the long term durability of the attachment strength of the stent to the graft after the equivalent of 10 years under physiologic load.	After attachment creep testing, the graft must withstand a worst-case transient load corresponding to a physiologic pressure of 320 mmHg. The device must be capable of sustaining a clinically relevant transient hypertensive physiological pressure of 320 mmHg after the equivalent of 10 years while maintaining a load corresponding to a physiologic pressure of 110 mmHg	Pass
10-yr Device Integrity – Stent Graft Creep	The confirm the continued functionality of the stent graft after 10 years of simulated graft creep under physiologic loads.	After creep testing, the graft must not burst below a pressure of 320 mmHg. Additionally, changes in either diameter or length must not alter the ability of the device to function. The device must be capable of sustaining a clinically relevant transient hypertensive physiological pressure of 320 mmHg after the equivalent of 10 years while maintaining a pressure of 110 mmHg	Pass
10yr Device Integrity – Stent Graft Pulsatile Fatigue	To confirm structural integrity of the stent graft under pulsatile blood pressure for the equivalent of a 10-year life.	The modular graft system (aortic body in combination with contralateral and ipsilateral iliac limbs and extensions) should provide structural integrity under pulsatile blood pressure for the equivalent of a 10-year life. The modular stent graft must withstand cyclic internal differential pressure loading from 80 to 120 mmHg for 400 million cycles. After cycling, the graft burst strength must remain greater than or equal to 320 mmHg.	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
10-yr Device Integrity – Graft Stent Attachment Fatigue 1) Angulated Graft-Stent Attachment Fatigue 2) Lesser Curve Graft-Stent Attachment Fatigue 3) Asymmetric Greater Curve Graft-Stent Attachment Fatigue	To evaluate the long-term durability of the aortic body stent graft and attachment for a 10-year life under 3 different clinically extreme conditions.	The aortic body graft - stent attachment sites must be able to transfer load from the graft to the stent for a 10-year life, and subsequently withstand a worst-case transient load corresponding to a physiologic pressure of 320 mmHg. The following test conditions define one of the anticipated clinical extreme conditions: 1) Angulated Graft-Stent Attachment Fatigue: The graft-stent attachment must withstand 400 million cycles of cyclic load corresponding to an 80 to 160 mmHg pressure differential, under worst case angulated conditions of 60 degree proximal neck angulation at a D/4 (i.e., diameter of aorta divided by 4) inner radius of curvature. 2) Lesser Curve Graft-Stent Attachment Fatigue: The graft-stent attachment must withstand 400 million cycles of cyclic load corresponding to a 0-80mmHg pressure gradient. These pressures simulate the relatively low (near compression) local loads observed on the lesser curve of an angulated aorta having neck angulation of 60 degrees at a D/4 (i.e., diameter of aorta divided by 4) inner radius of curvature. 3) Asymmetric Greater Curve Graft-Stent Attachment Fatigue: The graft-stent attachment must withstand 400 million cycles of cyclic load corresponding to an 80 -160mmHg pressure gradient assuming a worst-case anchor engagement of 25% of anchors engaged into the greater curve of an angulated aorta having proximal neck angulation of 60 degrees at a D/4 (i.e., diameter of aorta divided by 4) inner radius of curvature.	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
Stent Graft Radiopacity	To ensure the stent graft is visible under fluoroscopy during implant to allow for proper placement.	The implant must be visible under fluoroscopy during the implant procedure to allow for proper placement.	Pass
Stent Graft Length	To ensure the stent graft length meets the defined implant length.	The aortic body graft length will be 75±5 mm on the ipsilateral side and 80±5 mm on the contralateral side.	Pass
Aortic Body Stent Radial Force	To measure the stent radial force ensuring adequate stent to vessel barb engagement.	The radial force of the aortic body stent should meet the following criteria: minimum radial force of 0.4 lbf when the stent is compressed by a 2% diameter contraction and 0.2 lbf when the stent is at its maximum vessel diameter. The aortic body stent must transmit sufficient radial force and/or moment to embed the anchors into the aortic wall and thereby prevent migration of the graft.	Pass
Stent Graft Permeability	To determine the pressure required to force water through the aortic body graft material.	Graft water entry pressure (WEP) must not be less than a differential pressure of 817mmHg.	Pass
Stent Graft Inflation Channel Burst Strength	To confirm the aortic body graft inflation channels will not burst during graft inflation.	The aortic body graft inflation channels must not burst at a pressure differential less than 16 psi.	Pass
Stent Corrosion Resistance	To demonstrate that the stents and discrete attachments have adequate in vitro corrosion performance.	The stents must have *in vitro* corrosion performance that is at least equivalent to an FDA approved stent graft device.	Pass
Durability – Aortic Body Stent Maximum Strain by FEA	To confirm the stent design has adequate mechanical properties for manufacturing, delivery and fatigue performance.	Peak strains associated with belting the stent and tucking the anchors must be below 9% (determined analytically), and the alternating strain amplitude produced by the *in vivo* environment below ± 0.15% (i.e. 0.3% peak-to-peak) when determined by finite element analysis.	Pass

B. Animal Studies

The Alto™ Abdominal Stent Graft System shares the same basic design, materials of construction, and similar processing as the Ovation Abdominal Stent Graft System (P120006). Additionally, an earlier prototype of the Alto™ aortic body stent graft, which also shared construction of the same base materials, with similar processing, was used in animal studies to support approval of the CustomSeal™ Kit (P120006/S010) and the Ovation iX™ Iliac Stent Graft (P120006/S015).

These approved Ovation platform devices underwent previous animal testing and demonstrated acceptable results with respect to graft patency, absence of migration or kinking, absence of abnormalities on end-organ histopathology, and/or normal healing. Additionally, these devices have shown acceptable biocompatibility. Therefore, animal studies from these approved Ovation platform devices were leveraged in support of the Alto™ Abdominal Stent Graft System.

C. Biocompatibility

The biocompatibility assessment performed for the Alto™ Abdominal Stent Graft and Delivery System was based on ISO 10993-1:2009/Cor 1:2010, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process. The stent graft was classified as an implant device, permanent contact (> 30 days), while the delivery system was classified as an external communicating device, circulating blood, limited exposure (< 24 hours). All testing was performed by a qualified contract laboratory in accordance with FDA GLP Regulations, 21 CFR Part 58. The Autoinjector 2 was categorized as non-patient contacting. Therefore, it was determined that no biocompatibility testing was required.

Biocompatibility testing and results previously submitted for the Ovation Abdominal Stent Graft System (P120006), Ovation Prime Abdominal Stent Graft System (P120006/S001), CustomSeal™ Kit (P120006/S010) and Ovation iX™ Iliac Stent Graft (P120006/S015) were evaluated to determine their applicability to the requirements for the Alto™ Abdominal Stent Graft System. Device design, materials, construction and manufacturing / sterilization environment were taken into consideration.

Based on the assessment, previously conducted biocompatibility tests continue to be applicable to, and supportive of, the Alto™ Abdominal Stent Graft System. Any additional testing is summarized in **Table 6** and **Table 7** below.

Test methods were performed in accordance with the following, as referenced:

- ISO 10993-4: Selection of tests for interactions with blood
- ISO 10993-5: Tests for *in vitro* cytotoxicity
- ISO 10993-10 Tests for irritation and skin sensitization
- ISO 10993-11: Test for systemic toxicity
- ISO 10993-12: Sample preparation and reference materials
- American Society for Testing and Materials (ASTM) F756 – Standard Practice for Assessment of Hemolytic Properties of Materials
- Guidance for Industry and FDA Staff, *Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*, Section C Biocompatibility, subsection 1 Nickel ion release, issued on August 18, 2015

For the Alto™ Aortic Body Stent Graft, the biocompatibility testing conducted is provided in **Table 9** below.

Table 9: Alto™ Aortic Body Stent Graft –Biocompatibility Testing and Results

Test / Study Method	Test Purpose	Results	Conclusion
Cytotoxity – MEM Using L-929 Mouse Fibroblast Cells (FEP Aqueous Dispersion)	To evaluate the ability of the stent graft extracts to elicit a cytotoxic response in cultured mouse fibroblast cells. Stent grafts will be considered non-cytotoxic, if they score a level of 0, 1 or 2 at 24, 48 or 72±4 hours.	Non-cytotoxic Grade 0 cytotoxicity for test and negative controls Grade 4 for positive controls	Pass
Hemocompatibility – Hematology: ASTM (F756) Hemolysis Assay, Direct Contact and Extract Method (FEP Aqueous Dispersion)	To evaluate the hemolytic potential of stent grafts according to the ASTM guideline. Direct Contact and Extract Methods: Stent grafts will be considered non-hemolytic if the "Blank Corrected Hemolytic Index above the Negative Control %" is 0-2%.	Non-hemolytic – Stent grafts for Direct Contact and Extract Methods were shown to be non-hemolytic as the "Blank Corrected Hemolytic Index above the Negative Control %" were 0-2%.	Pass
***In Vitro* Nickel Ion Release (Nickel Elution Testing)** – on Nitinol of Alto™ aortic body graft	To determine whether leachables extracted from the stent grafts would cause toxicity at Day 1, Day 7 and Day 30.	Nickel levels were below the threshold of toxicity at Day 1, Day 7 and Day 30	Pass

For the Alto™ Aortic Body Delivery System, the biocompatibility testing conducted is provided in **Table 10** below.

Table 10: Alto™ Stent Graft Delivery System – Biocompatibility Test Results

Test / Study Method	Test Purpose	Results	Conclusion
Cytotoxicity – MEM Using L-929 Mouse Fibroblast Cells	To evaluate the ability of the delivery system extract to elicit a cytotoxic response in cultured mouse fibroblast cells.	Non-cytotoxic. Grade 0 cytotoxicity for test and negative controls Grade 4 for positive controls	Pass
Sensitization – ISO Guinea Pig Maximization Sensitization Test	To evaluate the potential of the delivery system extract to cause delayed dermal contact sensitization in a guinea pig.	No sensitization response – None of the test animals scored higher than a Grade 0 (Defined as "No visible change – No erythema or edema")	Pass
Irritation or Intracutaneous Reactivity - ISO Intracutaneous Reactivity	To determine if any chemicals that may leach or be extracted from the delivery system were capable of causing local irritation in the dermal tissues of the rabbit.	Non-irritant - Difference in extract dermal observations between the mean of the control and the mean of the test group was <1.0.	Pass
Systemic Toxicity (Acute) – ISO Acute Systemic Injection	To screen delivery system extracts for potential toxic effects as a result of a single-dose systemic injection in mice.	Non-toxic None of the animals showed signs of clinical toxicity, lost more than 10% of body weight, or had other adverse observations.	Pass
Hemocompatibility: Hematology – ASTM (F756) Hemolysis Assay, Direct Contact and Extract Method	To evaluate the hemolytic potential of the delivery system according to the ASTM guideline.	Non-hemolytic – Direct Contact Method –Delivery System Hemolytic Index is 0.0% and Negative control is 0.4% Positive control % Hemolytic Index is 84.9%. Extract Method –Delivery System and Negative control % Hemolytic Index is 0.0%. Positive control % Hemolytic Index is 88.8%	Pass
Hemocompatibility: Coagulation/Partial Thromboplastin Time (PTT)	To determine the potential of the delivery system to cause an effect on the coagulation cascade via the intrinsic coagulation pathway.	Non-activator of the intrinsic coagulation pathway. Average delivery system clotting time was 116% of the negative control while the average clotting time of the comparison article was 108% of the negative control.	Pass

Test / Study Method	Test Purpose	Results	Conclusion
Hemocompatibility: Coagulation/Platelet and Leukocyte Count	To determine if the delivery system exposed to whole blood would adversely affect the make-up of the platelet and leukocyte components of the blood.	After exposure to delivery system, Leukocyte and Platelet counts were not statistically different between the test and comparison articles.	Pass
Hemocompatibility: Complement Activation SC5b-9 Assay	To measure complement activation in Normal Human Serum (NI-IS) when serum is exposed to a delivery system.	The percent of normalized SC5b-9 concentration produced by the delivery system was 0.1-0.3% of the Cobra Venom Factor CVF, and comparison article was 0.2-0.3% of the CVF. Results were not statistically different from the negative reference material.	Pass
Pyrogen: Materials Mediated Rabbit Pyrogen	To determine whether an extract of the delivery system induced a pyrogenic response after hour 3 following intravenous injection in rabbits.	Non–pyrogenic – None of the rabbits had a temperature rise $\geqslant$ 0.5°C.	Pass
Hemocompatibility: Thrombogenicity	The Alto™ Aortic Body Delivery Catheter was evaluated for *in vivo* thrombogenicity by using data obtained during IDE study G160226. An analysis of that data concluded that incidence rates for thrombosis potentially emanating from the delivery catheter/blood interactions were lower than the average rates when compared to commercially approved EVAR devices.		

D. Sterilization / Packaging / Shelf Life Testing

Alto™ Aortic Body Stent Graft and Delivery System

The Alto™ Aortic Body Stent Graft and Delivery System is a single-use device that is provided sterile to the end user. The system is ethylene oxide (EO) sterilized and was adopted into the same validated EO sterilization process under the same contract sterilizer and built in the same manufacturing environment as the previously approved Ovation devices. The adoption test results demonstrate that the Alto™ Abdominal Stent Graft System meets AAMI TIR28:2009 requirements, including comparative resistance, EO residuals, bioburden levels and bioburden recovery efficiency, and pyrogen levels and can be adopted into the currently validated cycle. The sterilization process was validated to demonstrate a Sterility Assurance Level (SAL) of 10^{-6}.

The Alto™ Abdominal Stent Graft System utilizes the same packaging design / materials, similar configuration / labeling and sterilization cycles as those used for other approved Ovation devices, previously submitted packaging and labeling verification testing was leveraged in support of the packaging design for the Alto™ Abdominal Stent Graft System.

Testing of the Alto™ Abdominal Stent Graft System and its packaging were conducted to verify that the integrity and performance was not compromised due to the effects of packaging stress during transit. Test results passed requirements. A shelf life of 3 years has been established for the Alto™ Abdominal Stent Graft System based on product and package shelf-life testing.

Autoinjector 2

The Autoinjector 2 is electron beam sterilized using the same processes as the original Autoinjector (approved as part of the Ovation Abdominal Stent Graft System (P120006). Due to the similarities in design, sterilization re-validation was not required.

A shelf life of 3 years has been established for the Autoinjector 2 based on product and package shelf-life testing.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of endovascular aneurysm repair with the Alto™ Abdominal Stent Graft System for the treatment of infrarenal abdominal aortic aneurysms (AAAs) in the US under IDE G160226 and known as the ELEVATE Study. Data from this clinical study were the basis for the Panel-Track PMA Supplement approval decision.

The Alto™ Abdominal Stent Graft System is Endologix's next generation polymer-based abdominal stent graft system, based on the previously approved Ovation Abdominal Stent Graft Systems (i.e., Ovation, Ovation Prime, and Ovation iX™).

As the Alto™ Abdominal Stent Graft System is expected to perform similarly to Endologix's previously approved Ovation Abdominal Stent Graft Systems, this clinical study was designed to confirm that the device design modifications and modified Indications for Use, did not negatively impact clinical performance as compared to the clinical study conducted for the original Ovation Abdominal Stent Graft System, under IDE G090239.

Note: Information regarding the clinical evaluation of the previously approved Ovation Abdominal Stent Graft Systems can be found in the IFU for those devices.

A summary of the clinical study is presented below.

A. <u>Study Design</u>

Patients were treated between March 2017 and February 2018. The database for this Panel Track PMA Supplement reflected data collected through May 16, 2019 and included 75 patients. There were 13 investigational sites in the United States.

The study was a prospective, consecutively enrolling, single-arm, nonrandomized multicenter clinical study utilizing the Alto™ Aortic Abdominal Stent Graft System. The primary composite endpoint was defined as treatment success at 1 year relative to a performance goal of 80%, which represents a typical one-year performance threshold for EVAR devices. The primary effectiveness hypotheses were defined as:

$H_0: \pi \leqslant 0.80$ vs. $H_1: \pi > 0.80$

where π = the expected treatment success rate at 1 year. If the lower limit of the one-sided Clopper-Pearson 95% confidence interval for π is greater than 80%, then the null hypothesis for this analysis will be rejected in favor of the alternative indicating that treatment success is statistically significant above 80%.

A sample size of 75 patients was calculated based upon the primary effectiveness endpoint of treatment success at 1 year. It was estimated that 60 subjects with evaluable data at 1 year would provide 80% statistical power to test the primary hypothesis (estimated treatment success of 92.8% at 12 months) using a one-sided 95% confidence interval (Clopper-Pearson interval). This provided a more conservative estimate than the approximate method. Statistical analyses included standard descriptive statistics and the Kaplan-Meier method, with Kaplan-Meier curves generated for outcomes through 12 months.

The clinical study utilized the following independent oversight committees:

- Clinical Events Committee to adjudicate major adverse events (MAEs) and adverse events (AEs) reported by the sites as potentially related to the device;
- Core Laboratory - an independent imaging core laboratory to analyze computed tomography scans and x-rays for key baseline characteristics and effectiveness endpoints;
- Data Safety and Monitoring Board to provide ongoing study oversight of the safety of enrolled subjects.

1. Patient Screening and Enrollment

The patient screening process was as follows:

- The site consented the subject per their consent process.
- The site submitted the subject's computed tomography (CT) images to Endologix.
- Once received, subject CTs were reviewed by Endologix Imaging Services. Imaging Services evaluated the anatomical metrics of the subject against the inclusion/exclusion criteria and also the general suitability for EVAR. If the subject did not pass anatomical criteria, the subject was failed.

- If the subject passed Imaging Services, the CT was then reviewed by a Case Review Board (CRB). The CRB consisted of two vascular surgeons (i.e., the national principle investigator and the chief medical officer of Endologix). At least one CRB member was required to review a case. Site investigators received standing invitations to each CRB call and summaries of CT reviews were disseminated to the Site Investigators. The CRB reviewed the subjects' screening films for overall vascular suitability, such as excessive neck thrombus and a lack of proximal aortic neck.
- If both the CRB and Imaging Services deemed it appropriate, the site was given permission to enroll the subject.

A total of 140 subjects were screened for study inclusion with 75 subjects enrolled and 65 subjects rejected from study participation. The 65 excluded subjects were rejected by either: Imaging Services, CRB, or the Site Investigator. Twenty-five subjects were excluded by Imaging Services (on quantitative anatomic assessment of the CT). The most common reasons for study exclusion by Imaging Services were failure to meet juxtarenal aortic neck angulation ≤ 60º, patent iliac or femoral arteries that allow endovascular access with the Alto™ Abdominal stent graft system, and proximal aortic landing zone with an inner wall diameter of no less than 16mm and no greater than 30 mm at 7 mm below the inferior renal artery. Nineteen subjects were excluded by the CRB. The most common reasons for these patients being excluded were as follows: juxta-renal AAA, excess thrombus in the seal zone, narrow native bifurcation (<18mm), and aneurysm size being too small. Subjects could be excluded by the site investigator at any temporal point in the study. Twenty-one subjects were excluded by the Site Investigators. The most common reasons included: Site Investigator decision regarding subject anatomy, follow-up capabilities of subject and subject withdrawing consent. There were four subjects the site investigators determined were not appropriate candidates for the study due to anatomical reasons: one subject required hypogastric occlusion for common iliac aneurysm and the subject refused internal iliac artery coil embolization; one subject required sac embolization due to large lumbar arteries noted on preoperative CT; the Preop CT scan in one subject indicated that the upper right renal artery (RRA) was dominant, however on angiogram the right kidney was supplied equally from the upper and lower RRAs therefore an alternative AAA device was considered, and in one subject the physician determined the subject to have poor follow-up capabilities.

2. Clinical Inclusion and Exclusion Criteria

Inclusion Criteria

Enrollment in the ELEVATE study was limited to patients who met the following inclusion criteria:

1. Patient is ⩾ 18 years of age.
2. Patients who are male or non-pregnant female (females of childbearing potential must have a negative pregnancy test prior to enrollment into the study).
3. Patient has signed an Institutional Review Board (IRB)/Ethics Committee (EC) approved Informed Consent Form.
4. Patient is considered by the treating physician to be a candidate for elective open surgical repair of the AAA (i.e., category I, II, or III per American Society of Anesthesiology (ASA) classification. ASA category IV patients may be enrolled provided their life expectancy is greater than 1 year.
5. Patient has an infrarenal abdominal aortic aneurysm that meets at least one of the following:
   a. Abdominal aortic aneurysm ⩾5.0 cm in diameter
   b. Aneurysm has increased in size by 0.5 cm in last 6 months
   c. Maximum diameter of aneurysm exceeds 1.5 times the transverse dimension of an adjacent normal aortic segment*.

   *As part of the study, abdominal aortic aneurysms that are less than 5 cm in diameter may be treated, if at least one of the following anatomical criteria are met:
   - Aneurysm has increased in size by at least 0.5 cm in the last 6 months
   - Aneurysm is no less than 4 cm in diameter and exceeds 1.5 times the transverse dimension of an adjacent normal aortic segment, as demonstrated on the screening CTA, performed within 6 months of anticipated treatment.
6. Patient has patent iliac or femoral arteries that allow endovascular access with the Endologix, Inc. (Sponsor) Alto™ Abdominal Stent Graft System.
7. Patient has a proximal aortic landing zone with an inner wall diameter of no less than 16 mm and no greater than 30 mm at 7 mm below the inferior renal artery.
8. Patient has an adequate distal iliac landing zone with an inner wall diameter of no less than 8 mm and no greater than 25 mm.
9. Patient has an adequate distal iliac landing zone with a length of at least 10 mm. The resultant repair should preserve patency in at least one hypogastric artery.
10. Patient meets the following anatomic criteria: the distance from the most distal renal artery to most superior internal iliac artery measurement is at least 125 mm.
11. Patient has juxtarenal aortic neck angulation $\leq 60^{o}$ if proximal neck is $\geq$7 mm and $\leq$45 degrees if proximal neck is <7 mm.
12. Patient must be able and willing to comply with all required follow-up exams.

Exclusion Criteria

Patients were not permitted to enroll in the ELEVATE study if they met any of the following exclusion criteria:

1. Significant thrombus >8 mm in thickness; at any point along the aortic circumference at the level of 7mm below the inferior renal artery.
2. Diameter of aortic bifurcation that, in the physician's opinion, would compromise flow through the iliac limbs.
3. Patient has a dissecting aneurysm.
4. Patient has an acutely ruptured aneurysm.
5. Patient has an acute vascular injury.
6. Patient has a need for emergent surgery.
7. Patient has a known thoracic aortic aneurysm or dissection.
8. Patient has a mycotic aneurysm or has an active systemic infection.
9. Patient has unstable angina (defined as angina with a progressive increase in symptoms, new onset at rest or nocturnal angina, or onset of prolonged angina).
10. Patient has had a myocardial infarction (MI) and/or stroke (CVA) within the past 6 months.
11. Patient has a major surgical or interventional procedure planned 30 days prior and 30 days post procedure of the AAA repair.
12. Patient has history of connective tissue disease (e.g., Marfan's or Ehler's-Danlos syndrome).
11. Patient has history of bleeding disorders or refuses blood transfusions.
12. Patient has dialysis dependent renal failure or baseline serum creatinine level >2.0 mg/dl.
13. Patient has a known hypersensitivity or contraindication to anticoagulation or contrast media that is not amenable to pre-treatment.
14. Patient has a known allergy or intolerance to polytetrafluoroethylene (PTFE), PEG-based polymers, fluorinated ethylene propylene (FEP) or nitinol/ nickel.
15. Patient has a body habitus that would inhibit x–ray visualization of the aorta.
16. Patient has a limited life expectancy of less than 1 year.
17. Patient is currently participating in another investigational device or drug clinical trial.
18. Patient has other medical, social or psychological conditions that, in the opinion of the investigator, preclude them from receiving the pre-treatment, required treatment, and post-treatment procedures and evaluations.

3. Follow-up Schedule

All patients in the study were scheduled to return for follow-up examinations at 1 month, 6 months and 1 year postoperatively. Some patients returned for unscheduled

visits, which were incorporated into the clinical data set. Adverse events and complications were recorded at all visits.

Preoperatively – Preoperative assessment included a physical exam, an ankle-brachial Index (ABI) measurement, and laboratory testing, which included renal assessment, as well as serum pregnancy for female patients of childbearing potential.

Treatment period (implant/surgical procedure) – At the time of the endovascular procedure and prior to discharge, assessments were performed and data were collected on the following: type and length of anesthesia, type of vascular access, estimated blood loss, adjunctive procedures, volume of contrast used, total fluoroscopy time during procedure, investigator assessment of AAA device performance as it relates to delivery/deployment/required interventions, evidence of endoleak, device integrity issues, procedural times, and adverse events.

Post-Treatment follow-up visits (1 month, 6 months and 1 year) – The following post-treatment assessments were executed and documented:

- Physical examination
- Laboratory testing, which included renal assessment at 1month follow up visit
- Contrast-enhanced spiral abdominal/pelvic CT (in the event the subject was unable to tolerate a contrast-enhanced spiral CT, a duplex ultrasound and non-contrast spiral CT was completed as an alternative assessment)
- Abdominal x-ray (KUB), including AP, lateral, left oblique and right oblique views.

Additional assessments that were reported at each follow-up visit included:

- Type I endoleak, assessed by an Independent Core Lab
- Type III endoleak, assessed by an Independent Core Lab
- Stent graft migration > 10 mm (compared to 1-month baseline), assessed by an Independent Core Lab
- AAA enlargement > 5 mm (compared to 1-month baseline)
- Loss of patency
- Stent fracture, assessed by an Independent Core Lab
- AAA rupture
- Conversion to open repair
- Secondary interventions
- AAA-related mortality
- Adverse events, including:
    - Serious adverse events
    - Major adverse events
    - Procedure-related adverse events
    - Device-related adverse events

All adverse events, regardless of seriousness or cause

Table 11: Subject Follow-up Visit Schedule

Procedure	Baseline	Treatment	Discharge	1 Month Follow-Up	6 Months Follow-Up	1 Year Follow-Up
Medical/Surgical History	X[2]					
Physical Exam	X[2]		X	X	X	X
ABI	X					
Spiral Contrast Enhanced CT[5]	X[3]			X	X	X
Laboratory Assessments (BUN, Creatinine and Serum Pregnancy)[1]	X[1]			X[1]	X[1]	X[1]
Adverse Event Assessment		X	X	X	X	X
Device/aneurysm assessment based on imaging (endoleak, migration, integrity, patency)		X	X[4]	X	X	X

1 BUN, creatinine and serum pregnancy HCG required no more than 30 days prior to the implant/surgical for baseline. At every follow up time point beginning with 1 month follow up, only serum creatinine will be collected. *Note: the serum pregnancy is required for females of child-bearing potential only and only at baseline. BUN is only required at baseline.*

2 Baseline medical/surgical history and physical exam performed no more than 30 days prior to the implant/surgical procedure.

3 Baseline contrast enhanced CT must be obtained within 6 months of anticipated treatment date.

4 Only the device will be assessed via X-Ray at discharge as no CT is performed at that visit.

5 Note that in the event the subject is unable to tolerate a contrast-enhanced spiral CT, a duplex ultrasound and non-contrast spiral CT should be completed as an alternative assessment.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

4. Clinical Endpoints

With regards to safety, the incidence rate of Major Adverse Events (MAEs) following AAA repair were evaluated at 30 days, 6 months and 1 year. MAEs were defined as death (i.e., all-cause mortality, AAA-related mortality); myocardial infarction; stroke; renal failure; respiratory failure; paralysis; bowel ischemia; procedural blood loss (> 1,000 cc). All MAEs were adjudicated by an independent clinical events committee (CEC). Other safety variables collected and analyzed comprised of adverse events,

which included serious adverse events, major adverse events, procedure-related adverse events, device-related adverse events and all other adverse events, regardless or seriousness or cause.

With regards to effectiveness, the primary composite endpoint was defined as treatment success at 12 months, which included technical success (i.e., a composite endpoint of successful delivery, successful and accurate deployment, and successful withdrawal) and freedom from AAA enlargement, stent graft migration, type I or III endoleak, AAA rupture or surgical conversion, stent graft stenosis, occlusion or kink requiring a secondary intervention, any thromboembolic event attributable to stent graft requiring secondary intervention, and stent fracture requiring secondary intervention.

With regard to success/failure criteria, the study would be considered successful if the performance goal of 80% for treatment success at 12 months for the primary composite endpoint was met.

B. Accountability of PMA Cohort

At the conclusion of the study, of the 75 patients enrolled, all 75 were available at 1 month follow-up (1 died, 2 withdrew consent after 1 month follow-up but before the 6 month follow-up); 72 patients were eligible at 6 month follow-up (2 died, 1 withdrew consent, and 1 was converted to open repair after the 6-month follow-up but before the 12 month follow-up) and 68 subjects were eligible at 12 months. Sixty seven (67) subjects completed a 1-year follow-up visit and, of these 61 were evaluable for the primary composite endpoint.

Table 12: Subject and Imaging Accountability Through 12 Month Follow- Up Visit (Alto™ Treatment Group – All Subjects)

							Imaging compliance											
							CT						X-ray					
									Adequate imaging to assess the parameter n (% of eligible) §					Adequate imaging to assess the parameter n (% of eligible)		Events occurring before next interval			
Visit	Eligible for follow-up*	Subjects with follow-up	Overdue (Past) †	Missed Visit‡	In window, follow-up pending¥	Not due for next visit€	Site Performed@	Corelab Reviewed#	Size Increase (Per Corelab)	Endoleak (Per Corelab)	Migration (Per Corelab)	Patency (Per Site)	Corelab Reviewed	Fracture	Other Stent Finding	LTF or WD	Died	Conversion	Conversion + Died
Operative	75	75	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	68 (90.7%)	68 (90.7%)	68 (90.7%)	0	0	0	0
1 Month	75	75 (100.0%)	0	0	0	0	74 (98.7%)	74 (100.0%)	74 (98.7%)	73 (97.3%)	74 (98.7%)	74 (98.7%)	70 (93.3%)	70 (93.3%)	70 (93.3%)	2	1	0	0
6 Month	72	72 (100.0%)	0	0	0	0	72 (100.0%)	72 (100.0%)	72 (100.0%)	70 (97.2%)	72 (100.0%)	72 (100.0%)	69 (95.8%)	69 (95.8%)	69 (95.8%)	1	2	1	0
1 Year	68	67 (98.5%)	1**	0	0	0	63 (92.6%)	65 (103.2%)$	64 (94.1%)	61 (89.7%)	64 (94.1%)	64 (94.1%)	61 (89.7%)	61(89.7%)	61 (89.7%)	0	0	0	0

*Eligible for follow-up = Subjects with follow-up + Overdue + Missed visit. Does not included those with follow-up pending, not yet due for the visit, previous deaths, conversions, and those lost to follow-up (LTF) or withdrawn (WD).

†Subjects without a follow-up visit but not yet in next window

‡ Subjects without a follow-up visit and currently in next window

¥ Subjects currently in window, but data not yet available

€ Subjects not yet in the window

§These counts reflect the number of subjects with adequate imaging as determined by Core Lab.

** This single subject was classified as overdue because the exit was on post-op day 455 and was therefore considered enrolled during the duration of the 1-year follow-up period. As there were no follow-up windows available beyond one year, the status is not classified as a missed visit.

@Within each visit window, the "Site Performed" and 4 variables under "Adequate Imaging" all use the number of "Eligible" subjects as the denominator. On occasion the number of subjects with adequate imaging for a specific variable may be higher or lower than the "Site Performed" frequency, as the latter only counted images of the required type (Contrast CT or Non-Contrast CT + Duplex Ultrasound). As an example a site may not obtain a CT but still perform an ultrasound. This was not considered a compliant imaging visit for the site and thus it was not counted in the "Site Performed" column. Yet there still may be sufficient information for specific variables such as sac size, so the image was counted in those columns where evaluable information was gathered.

#The "Corelab reviewed" column represents the number of CTs/US reviewed by the corelab, and uses the number of adequate images within the "Site Performed" column as the denominator. On occasion more images were reviewed by the corelab than compliant images obtained by the site.

$One subject was recorded as only having an ultrasound and no CT at 1 year (the corelab reviewed the Ultrasound). Another subject did not have a contrast CT recorded by the site in the dataset, though the Corelab evaluated a non-contrast CT. The percentage was greater than 100% for the 1 year visit because two subjects did not have the required imaging type, but were captured under corelab reviewed

C. Study Population Demographics and Baseline Parameters

1. Demographics

The demographics of the patient population are typical for an endovascular stent graft study performed in the US and are summarized in **Table 13** below. Most subjects enrolled in the study were male (93%), elderly (mean age: approximately 73 yr.), and white/not Hispanic or Latino (77%).

Table 13: Subject Demographics

Variable	Statistic	Alto™ Treatment Group
	N	75
Age (years)	Mean ± std	73 ± 7
Calculated Body Mass Index (BMI), (kg/m^2)	Mean ± std	30 ± 7
Gender		
Male	% (n/N)	93% (70/75)
Female	% (n/N)	7% (5/75)
Race/Ethnicity		
White / Not Hispanic or Latino	% (n/N)	77% (58/75)
White / Hispanic or Latino	% (n/N)	1% (1/75)
Black or African American / Not Hispanic or Latino	% (n/N)	1% (1/75)
Unknown / Not Hispanic or Latino	% (n/N)	15% (11/75)
Unknown / Hispanic or Latino	% (n/N)	1% (1/75)
Unknown / Unknown	% (n/N)	4% (3/75)

2. Subject Medical History

Baseline data regarding subject medical history is summarized in **Table 14** below. Subjects presented with typical comorbidities observed in AAA patients, most commonly hypertension 83% (62/75), hyperlipidemia 76% (57/75), and smoking history 75% (56/75). Subjects were risk-classified using the American Society of Anesthesiology (ASA) criteria with most presenting as ASA class III and IV 93% (70/75).

Table 14: Subject Medical History

Variable	Alto™ Treatment Group % (n/N)
ASA Grade	
1/2	5 (7%)
3/4	70 (93%)

Variable	Alto™ Treatment Group % (n/N)
Cardiovascular History	72/75 (96%)
Coronary artery disease	35/75 (47%)
Valvular heart disease	11/75 (15%)
Angina pectoris or chest discomfort	5/75 (7%)
Cardiomyopathy	3/75 (4%)
Congestive heart failure	6/75 (8%)
Myocardial infarction	11/75 (15%)
Arrhythmia	17/75 (23%)
Hypertension	62/75 (83%)
Hypotension	0 (0%)
Hyperlipidemia	57/75 (76%)
Peripheral Vascular, Stroke, and Aneurysm History	75/75 (100%)
Peripheral vascular disease	13/75 (17%)
Carotid artery disease	6/75 (8%)
Transient Ischemic Attack (TIA)	4/75 (5%)
Stroke	0 (0%)
Family history of aneurysms	9/75 (12%)
Pulmonary History	71/75 (95%)
Tobacco use (Current)	15/75 (20%)
Tobacco use (Former)	56/75 (75%)
COPD	27/75 (36%)
Gastrointestinal, Genitourinary, Reproductive History	49/75 (65%)
Renal insufficiency	5/75 (7%)
Endocrine	31/75 (41%)
Diabetes (Type II)	22/75 (29%)
Hematological	9/75 (12%)
Anemia	5/75 (7%)
Psychosocial	11/75 (15%)
Depression	7/75 (9%)
Alcohol	3/75 (4%)
Other significant medical history	26/75 (35%)

3. Subject Vascular Characteristics

Baseline data regarding subject vascular characteristics is summarized in **Table 15** below. Baseline Vascular characteristics were reported by Endologix Imaging Services

exclusively. All subjects enrolled in this study met the inclusion criteria based on Imaging Services CT measurements. Mean AAA diameter was 51.7 mm, with a mean proximal neck length of 27.9 mm. External iliac diameters measured 8.2 ± 1.7mm on the left, and 8.1 ± 1.5mm on the right.

Table 15: Vascular Characteristics

Variable	Statistic	N	Alto™ Treatment Group*
Juxtarenal Angle (°)		75	23.1 ± 18.7
Aortic diameter Inferior Renal-35mm [1]	Min (mm)	75	25.0 ± 2.3
	Max (mm)	75	26.6 ± 2.4
	Average (mm)	75	25.9 ± 2.3
Aortic diameter Inferior Renal (or intended position)	Min (mm)	75	21.8 ± 2.5
	Max (mm)	75	23.2 ± 2.6
	Average (mm)	75	22.5 ± 2.5
Aortic diameter Inferior Renal + 7mm	Min (mm)	75	21.8 ± 2.3
	Max (mm)	75	23.0 ± 2.7
	Average (mm)	75	22.4 ± 2.4
Change from Inferior Renal to Inferior Renal+7 (%)		75	0.0 ± 7.2
Aortic diameter Inferior Renal + 10mm	Min (mm)	75	21.8 ± 2.5
	Max (mm)	75	23.4 ± 2.8
	Average (mm)	75	22.6 ± 2.5
Maximum Sac Diameter (mm)		75	51.7 ± 6.6
<40 mm[#]		4	5%
⩾40, <50 mm		23	31%
⩾50, <60 mm		40	53%
⩾60 mm		8	11%
Native Bifurcation	Min (mm)	74	20.1 ± 5.1
	Max (mm)	74	26.2 ± 6.7
Transverse dimension of adjacent normal aortic segment (mm)		27	22.7 ± 4.1
Neck Length (mm)		75	27.9 ± 13.7
Distance from the most distal renal artery to most superior left internal iliac artery (mm)		75	182.5 ± 24.7
Distance from the most distal renal artery to most superior right internal iliac artery (mm)		75	181.2 ± 21.0
Inferior Renal to Aortic Bifurcation (mm)		75	110.9 ± 13.1
Right Distal Iliac Diameter	Min (mm)	75	15.8 ± 3.8
	Max (mm)	75	17.1 ± 4.0

	Average (mm)	75	16.5 ± 3.9
Right External Iliac Diameter	Min (mm)	75	7.6 ± 1.6
	Max (mm)	75	8.7 ± 1.6
	Average (mm)	75	8.1 ± 1.5
Left Distal Iliac Diameter	Min (mm)	75	15.1 ± 3.0
	Max (mm)	75	16.4 ± 3.3
	Average (mm)	75	15.8 ± 3.1
Left External Iliac Diameter	Min (mm)	75	7.6 ± 1.9
	Max (mm)	75	8.7 ± 1.6
	Average (mm)	75	8.2 ± 1.7
Left Distal Iliac landing zone (mm)		75	49.1 ± 18.7
Right Distal Iliac landing zone (mm)		75	50.1 ± 20.7
SIR Calcification Grade[2] Calcification 0% of circumference		14	19%
Calcification <25% of circumference		49	65%
Calcification 25-50% of circumference		11	15%
Calcification >50% of circumference		1	1%
SIR Thrombus Grade[2] Thrombus 0% of circumference		27	36%
Thrombus <25% of circumference		16	21%
Thrombus 25-50% of circumference		18	24%
Thrombus >50% of circumference		14	19%

*Results are presented as mean ± SD (min, max) [med] or % of total responses.

4 patients were enrolled that had AAA diameters <40mm. All these four patients were enrolled under Rev A (under Rev A, this was not an inclusion exclusion violation). After this the protocol was amended under Revision B where subjects with AAA diameter <40mm could not be enrolled. No other subjects with AAA diameter <40mm were enrolled in the study after the corrective memo was distributed.

[1] Data provided by site imaging

[2] Proximal neck calcification and thrombus scoring: Amount of calcium and/or thrombus present in the cross-sectional area of the target location of the sealing ring (OR+4 to IR+10).

4. Devices Implanted

A total of 75 Alto™ Abdominal Stent Graft System aortic bodies, 155 Ovation iX™ Iliac Limbs, and 7 Ovation iX™ Iliac Extensions were implanted in 75 subjects during the initial implant procedure. All subjects received at least one aortic body and two iliac limbs. Additional iliac limbs and iliac extensions could be used to extend the length of the device, where indicated. Four subjects had bilateral limb extensions. Four subjects had unilateral limb extensions (three on the left side and one on the right) Seven iliac extensions were used, and 5 iliac limbs were used as extensions. One subject had a Balloon Expandable Stent implanted at day 48 to treat a Type Ia endoleak.

Alto™ aortic body stent grafts and Ovation iliac limbs (including iliac extensions), delivery and deployment were successful in all subjects.

The summary of Alto™ components implanted is presented in **Table 16** below. Device use by size is presented in **Table 17** below.

Table 16: Summary of Alto™ Components Implanted

Alto™ Components	**Alto™ Treatment Group % (n/N)**
Aortic Body	100% (75/75)
Ipsilateral limb	100% (75/75)
Contralateral limb	100% (75/75)
Iliac extension	9.3% (7/75)
Ipsi/contra limb used as extension	7.0% (5/75)

Table 17: Distribution of Implanted Device Sizes

Device Type	**Diameter**	**Alto™ Treatment Group % (n/N)**
Aortic Body		75
	20	0.0% (0/75)
	23	18.7% (14/75)
	26	45.3% (34/75)
	29	29.3% (22/75)
	34	6.7% (5/75)
Iliac Limb		155*
	10	1.3% (2/155)
	12	9.7% (15/155)
	14	14.2% (22/155)
	16	26.5% (41/155)
	18	21.3% (33/155)
	22	18.7% (29/155)
	28	8.4% (13/155)
Iliac Extension		7
	10	0.0% (0/7)
	12	0.0% (0/7)
	14	0.0% (0/7)
	16	14.3% (1/7)

Device Type	Diameter	Alto™ Treatment Group % (n/N)
	18	57.1% (4/7)
	22	14.3% (1/7)
	28	14.3% (1/7)

[*]Five iliac limbs were used as extensions.

5. Acute Procedural Information

The following secondary clinical utility endpoints were collected and are shown in **Table 18**. Bilateral percutaneous access was achieved in 90.7% (68/75) of subjects and 33.3% (25/75) of subjects did not require general anesthesia. The endovascular procedure was, on average, 90 minutes in duration with minimal blood loss (mean: 52.5 mL) and required a short hospital stay (mean: 1.3 day). 26.7% of subjects (20/75) were admitted to the ICU. Among subjects that went to the ICU, the mean was 0.9 days of stay in ICU. Mean fluoroscopy time was 20 minutes. Technical success (successful device delivery, deployment, and withdrawal) was achieved in 100% of cases.

Table 18 – Procedural Information

Variable	Statistic[*]	Alto™ Treatment Group
Total Procedure time (min)	N	75
	Median	90
	Min, Max	41, 241
< 90 min	% (n/N)	49.3% (37/75)
⩾ 90 min, < 150 min	% (n/N)	44.0% (33/75)
⩾ 150 min, < 210 min	% (n/N)	5.3% (4/75)
⩾ 210 min	% (n/N)	1.3% (1/75)
Estimated Procedural Blood Loss (mL)	N	72
	Median	52.5
	Min, Max	10, 1000
Length of hospital stay (days)	N	75
	Median	1.3
	Min, Max	0.2, 20.2
Duration of ICU stay (among subjects admitted to ICU, in days)	N	20
	Median	0.9
	Min, Max	0.6, 1.3

Variable	Statistic*	Alto™ Treatment Group
Anesthesia Type	N	75
General	% (n/N)	66.7% (50/75)
Regional	% (n/N)	1.3% (1/75)
Local with Conscious Sedation	% (n/N)	32.0% (24/75)
Total Anesthesia time (min)	N	50
	Median	147
	Min, Max	86, 316
< 90 min	% (n/N)	2.0% (1/50)
⩾ 90 min, < 150 min	% (n/N)	50.0% (25/50)
⩾ 150 min, < 210 min	% (n/N)	28.0% (14/50)
⩾ 210 min	% (n/N)	20.0% (10/50)
Fluoroscopy time (min)	N	75
	Median	20
	Min, Max	6,46
< 10 min	% (n/N)	6.7% (5/75)
⩾ 10 min, < 20 min	% (n/N)	42.7% (32/75)
⩾ 20 min, < 30 min	% (n/N)	28.0% (21/75)
⩾ 30 min	% (n/N)	22.7% (17/75)
Aortic Body Access	N	75
Percutaneous	% (n/N)	94.7% (71/75)
Cut-down	% (n/N)	5.3% (4/75)
Technical Success@	% (n/N)	100% (75/75)

*Results are presented as Median (Min, Max), or as % of total responses.

@ Technical Success is defined as:

Successful delivery, defined as ability to deliver the implant to the intended location without the need for unanticipated corrective intervention related to delivery, using an adjunctive device outside of the Alto™ Abdominal Stent Graft System;

Successful and accurate deployment, defined as:

- deployment of the endovascular stent graft in the planned location
- patency of the endovascular stent graft, absence of device deformations (e.g. kinks, stent eversion, mal-deployment, misaligned deployment) requiring unplanned placement of an additional device within the endovascular stent graft

Successful withdrawal of the delivery system without the need for unanticipated corrective intervention related to withdrawal

One subject had a hospitalization time of 20.2 days. This subject was admitted to hospital one day before the scheduled AAA repair due to a fall. The subject had some complications due to the fall and was kept in the hospital. The subject had the procedure on day 15 of being in the hospital. The subject was a 73-year-old male who presented with HTN, HLD, tobacco use, morbid obesity, diabetes, peripheral vascular disease and ASA III who underwent successful implantation of the Alto™ Abdominal Stent Graft System in a 65.6mm infrarenal aortic aneurysm. Intra-procedurally, the subject experienced blood loss of 1L due to access difficulties resulting in surgical cutdown and 2u PRBC transfused. Despite a difficult pre-operative course, there were no subsequent post-operative complications, and the subject was discharged on post-operative day 5 in good condition. The event was assessed as unrelated to the device by both the site and CEC. The subject successfully completed study follow-up and exited after completing the 1-year follow-up visit.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the incidence rate of Major Adverse Events (MAEs) on evaluable patients at 30 days, 6 months and 1 year. MAEs were defined as any of the following variables: death (i.e., all-cause mortality, AAA-related mortality); myocardial infarction, stroke, renal failure, respiratory failure, paralysis, bowel ischemia, or procedural blood loss $\geqslant$ 1,000 cc. Evaluation of these variables were descriptive. No hypothesis testing was performed for these variables.

In addition to the MAEs, other key safety outcomes for this study are presented in the tables below.

1.1 MAJOR ADVERSE EVENTS (MAEs) THROUGH 30 DAYS (PRIMARY SAFETY ENDPOINT) AND 365 DAYS

The incidence of MAEs through 365 days, per CEC adjudication, was 10.7% (8/75). Major MAEs were reported in 4 subjects (5.3%) within 30 days post-treatment and 4 subjects (5.3%) from 31 to 365 days. No subject had more than one event. Three subjects experienced bowel ischemia on post-operative days 1, 5, and 5 respectively. All three cases of bowel ischemia were adjudicated to be related to the procedure and not related to the device. Per the CEC, two of the subjects had anatomical factors that might have pre-disposed them to these events. One subject with bowel ischemia required no management to treat. One subject required a colonoscopy and clear liquid diet. One subject had a superior mesenteric artery (SMA) angioplasty attempted but not completed due to difficulty with passage of catheters adjacent to suprarenal struts and findings of an 18mm pressure gradient. Subsequently, the subject's symptoms resolved. All three subjects that experienced

bowel ischemia completed 1-year follow-up (with no additional events or secondary interventions reported).

There was one subject that experienced procedural blood loss greater than 1,000 mL on post-operative day 0. The Clinical Events Committee (CEC) adjudicated this to be procedure related, and not related to the device. There were three deaths reported in the study. One subject died on post-operative day 97 due to unknown cause. One subject died on post-operative day 225 due to lung cancer, and another subject expired on post-operative day 248 due to complications of extremity trauma. All three deaths were adjudicated to not be procedure or device related. There was one subject that experienced a myocardial infarction (that did not lead to death) on post-operative day 225. This event was adjudicated to not be related to the device or procedure. The subject completed the study. There were no instances of paralysis, renal failure, respiratory failure, or stroke reported. Refer to **Table 19** below.

Table 19 - MAE Rates through 365 Days

Major Adverse Events (MAEs) within 1 Year			
Major Adverse Events	**⩽30 days**	**31 Days-1 Year**	**Total within Year 1**
Subjects with ⩾1 MAE	5.3% (4/75)	5.3% (4/75)	10.7% (8/75)
Death	0%	4.0% (3/75)	4.0% (3/75)
Bowel Ischemia	4.0% (3/75)	0%	4.0% (3/75)
Myocardial Infarction	0%	1.3% (1/75)	1.3% (1/75)
Paralysis	0%	0%	0%
Renal Failure	0%	0%	0%
Respiratory Failure	0%	0%	0%
Stroke	0%	0%	0%
Procedural blood loss ≥ 1000 cc	1.3% (1/75)	0%	1.3% (1/75)

1.2 ALL-CAUSE MORTALITY THROUGH 365 DAYS

All-cause mortality through 365 days post-treatment was 4.0% (3/75). The deaths were due to unknown cause (day 97), lung cancer (day 225), and complications of extremity trauma (day 248). All deaths were adjudicated by the CEC as unrelated to the device and procedure. Freedom from all-cause mortality was estimated to be 100% at 30 days, 98.7% at 180 days, and 95.9% at 365 days. There were no AAA-related deaths in the study through 365 days. Refer to **Table 20** below.

Table 20: All-Cause Mortality Rates through 365 Days

All-Cause Mortality within 1 Year			
Variable	**⩽30 Days**	**31-365 Days**	**0-365 Days**
Death (All-cause)	0%	4.0% (3/75)	4.0% (3/75)

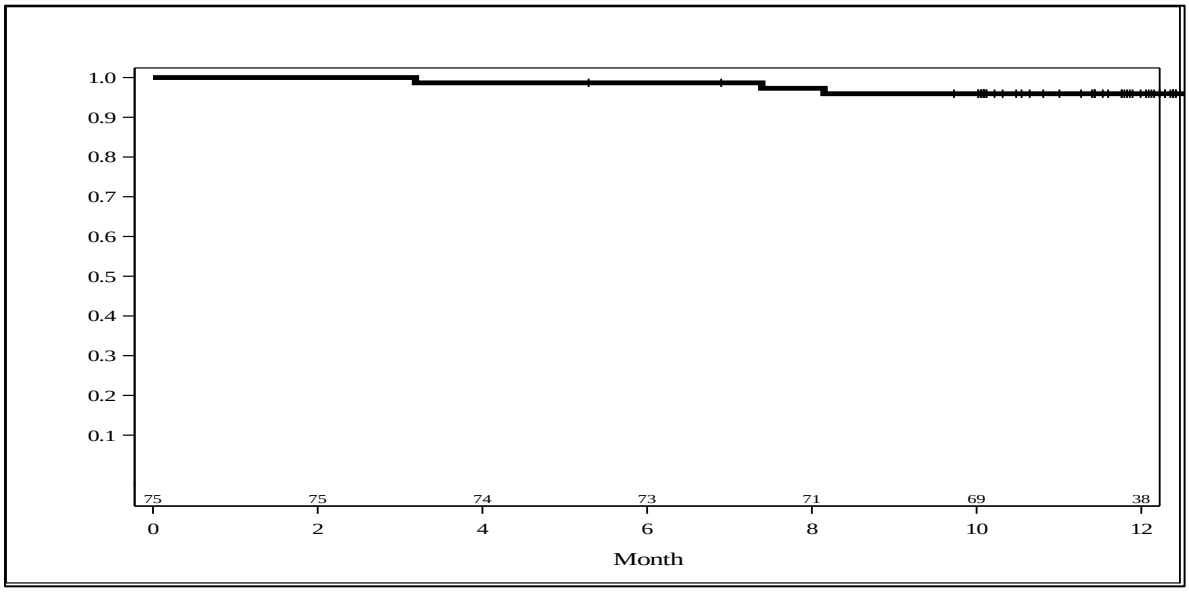
The Kaplan-Meier estimate of freedom from all-cause death through 365 days was 95.9%. Refer to **Table 21** and **Figure 6** below.

Table 21:Freedom from All-Cause Mortality through 365 Days: Kaplan-Meier Estimate

Variable	Treatment to 30 days	31 to 180 days	181 to 365 days
Number at risk[1]	75	75	73
Number of events[2]	0	1	2
Number censored[3]	0	1	33
Kaplan-Meier estimate[4]	100	98.7	95.9
Standard error	0	1.3	2.3

1 Number of subjects at risk at beginning of interval
2 All events within the time interval
3 Subjects are censored on the current post-op day as of the date of the data-cut, having completed the study, or upon exit or loss to follow-up
4 Estimate at the end of the time interval

Figure 6: Freedom from All-Cause Mortality through 365 Days: Kaplan-Meier Estimate



1.3 AAA- RELATED MORTALITY THROUGH 12 MONTHS

No AAA-related deaths were reported through 365 days post treatment.

1.4 AAA RUPTURE THROUGH 12 MONTHS

No AAA ruptures were reported through 365 days post treatment.

1.7 DEVICE-RELATED ADVERSE EVENTS

A device-related adverse event was defined as any event that was adjudicated by the CEC as related to the device. Device-related AEs were reported in 2.7% (2 of 75) of subjects through 365 days post-treatment.

A Type IA endoleak was reported for one subject in the 30-day window. The Type IA endoleak remained after the Alto™ Abdominal Stent Graft System was ballooned three times. At the 1-month follow-up visit the Type IA endoleak was found to persist. The AAA sac size decreased from 55mm preoperatively to 53.1mm at 1 month. The endoleak was treated on day 48 with an Endologix Balloon Expandable Stent (BES) (30mm diameter) which was placed at the proximal neck inside the Alto™ Abdominal Stent Graft System (note that Endologix is not seeking commercialization of this BES at this time). The procedure was successful and the endoleak resolved. This event was counted against the primary composite endpoint.

A device-related serious adverse event (SAE) of device infection was seen in another subject at Day 268. The subject was admitted to the hospital where he presented with abdominal and back pain and nausea, for which a CT taken confirmed the presence of a device infection on the aortic body. The patient underwent emergent conversion to open repair on post-operative day 273, and surgical AAA repair with a tissue homograft. The Alto™ device was explanted and returned to the sponsor for evaluation. The subject was discharged on post-explant day 11 in good condition. The subject subsequently exited the study on post-operative day 296. The CEC adjudicated the adverse event as related to the Alto™ device, although they considered the infection to be opportunistic.

The incidence of device-related adverse events is presented in **Table 22** below.

Table 22: Device-related Adverse Events through 365 Days

System Organ Class	⩽30 days	31-365 Days	0-365 Days
Infections and Infestations	0	1 1.3% (1/75)	1 1.3% (1/75)

System Organ Class	⩽30 days	31-365 Days	0-365 Days
Type I endoleak	1 1.3% (1/75)	0	1 1.3%
Total Subjects	1 1.3% (1/75)	1 1.3% (1/75)	2 2.7% (2/75)

1.8 PROCEDURE-RELATED ADVERSE EVENTS

A procedure-related adverse event was defined as any event that was adjudicated by the CEC as related to the procedure for adjudicated events, or was procedure related in the investigator's opinion for events not adjudicated. Procedure-related AEs were reported in 12.0% (9 of 75) of subjects through 365 days post-treatment.

One event was a Type 1A endoleak (discussed in Section 1.7 above). The other two were both Type II endoleaks (neither were considered device related).

The incidence of procedure-related adverse events is presented in **Table 23** below.

Table 23: Procedure-related Adverse Events through 365 Days

Procedure Related Events* (n=75)			
System Organ Class	**⩽30 days**	**31-365 Days**	**0-365 Days**
Gastrointestinal Disorders	2 (2.7%)	0	2 (2.7%)
General Disorders and Administration Site Conditions	0	2 (2.7%)	2 (2.7%)
Injury, Poisoning and Procedural Complications	3 (4.0%)	0	3 (4.0%)
Type IA Endoleak	1 (1.3%)	0	1 (1.3%)
Aneurysm Expansion	0	1 (1.3%)	1 (1.3%)
Total Subjects	6 (8.0%)	3 (4.0%)	9 (12.0%)

**A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory.*

1.9 UNANTICIPATED ADVERSE DEVICE EVENTS

No Unanticipated Adverse Events were reported through 365 days post treatment.

2. Effectiveness Results

The analysis of effectiveness was based on the 61 evaluable subjects at 1-year. Key effectiveness outcomes are presented in the following tables below.

2.2 *TREATMENT SUCCESS*

Treatment success (the primary composite endpoint), defined as technical success *and* freedom from: AAA enlargement, stent graft migration, type I or III endoleak, AAA rupture, surgical conversion, stent graft stenosis, occlusion or kink requiring a secondary intervention, any thromboembolic events attributable to stent graft requiring secondary intervention, and stent fracture requiring secondary intervention through 1 year was 95.1% (**Table 24**). The primary study endpoint of treatment success was met.

Table 24: Primary Endpoint: Treatment Success

Variable	Alto™ Treatment Group % (n/N)	Lower one-sided 95% Confidence Limit*	Target Performance Goal	Study Endpoint
Treatment success	95.1% (58/61)	87.8%	80%	MET

Given that 14 of 75 subjects were enrolled in the study but lacked the appropriate information to evaluate the primary endpoint, a post-hoc sensitivity analysis was conducted to calculate the Kaplan-Meier estimate of the primary endpoint. The Kaplan-Meier estimate of the primary endpoint shows 96.8% freedom from failure at 1-year, which is comparable to the prespecified primary analysis finding of 95.1%.

For the treatment success endpoint, technical success was defined as a composite endpoint of successful delivery, successful and accurate deployment, and successful withdrawal. Successful delivery was defined as ability to deliver the implant to the intended location without the need for unanticipated corrective intervention related to delivery, using an adjunctive device outside of the Alto™ Abdominal Stent Graft System. Successful and accurate deployment was defined as deployment of the endovascular stent graft in the planned location and patency of the endovascular stent graft, absence of device deformations (e.g. kinks, stent eversion, mal-deployment, misaligned deployment) requiring unplanned placement of an additional device within the endovascular stent graft. Successful withdrawal of the delivery system was achieved without the need for unanticipated corrective intervention related to withdrawal. Technical success was obtained in 100% of patients (75 of 75).

There were three subjects that failed the endpoint defined below (**Table 25**). One subject had a conversion to open repair on day 273 post-implant, due to a device infection. One additional subject was noted to have aneurysm expansion (5.9mm) in the 1-year imaging window. This event was adjudicated by the CEC as likely due to a type II endoleak. An additional subject had a type IA endoleak present at the 30-day follow-up which was subsequently corrected by a balloon expandable stent on post-op day 48. The CEC adjudicated the event as related to the device.

Table 25: Treatment Success to 1 Year

Outcome	Result
	(n=61)
Total Subjects with Treatment Success	58 (95.1%)
Total Subjects with Treatment Failure	3 (4.9%)
Procedural technical failure	0 (0.0%)
Aneurysm rupture	0 (0.0%)
Conversion to open repair	1 (1.6%)
Secondary interventions	0 (0.0%)
Aneurysm sac expansion	1 (1.6%)
Clinically significant migration	0 (0.0%)
Type I endoleak*	1 (1.6%)
Type III endoleak	0 (0.0%)

*****One subject had a Type Ia endoleak present at the 30-day follow-up and was treated and corrected with a Balloon Expandable Stent (secondary intervention) on post-op day 48.

2.3 AAA ENLARGEMENT

Aneurysm enlargement, defined by the Independent Core Lab, as a >5 mm AAA diameter increase compared to the AAA diameter measured on the 1-month CT scan (baseline), was reported in 1.6% (1 of 61) of subjects (See **Table 26**.) One subject was reported as having an aneurysm expansion of 5.9mm at the 1-year follow-up visit. The site noted this as an adverse event (AE) at the 6-month follow-up visit. The CEC adjudicated the aneurysm expansion as likely due to a type II endoleak. This event was also adjudicated to be serious, related to the procedure, and unrelated to the device. Subject exited the study successfully without any secondary interventions to treat aneurysm expansion.

Aneurysm decrease was defined as a >5mm AAA diameter decrease, whereas a change in AAA diameter ± 5mm in either direction was defined as stable. At 1 year, AAA diameter decrease was reported in 21.3% (13 of 61) of subjects.

See **Table 26** below for Core Lab reported sac diameter changes.

Table 26: Core Lab Reported Sac Diameter Changes through 12-Months

	Sac Diameter at Visit		Sac Diameter Change from 1 Month				
Timepoint	N	Sac Diameter (mm)	N*	Decreased (>5 mm)	Stable (±5 mm)	Increased (>5 mm)	No Growth
Screening	75	51.7 ± 6.6	N/A	N/A	N/A	N/A	N/A
1 Month	74	51.1 ± 7.0	N/A	N/A	N/A	N/A	N/A
6 Months	72	49.6 ± 7.3	69	7 (10.1%)	62 (89.9%)	0 (0.0%)	69 (100.0%)
12 Months	64	49.0 ± 8.3	61	13 (21.3%)	47 (77.0%)	1 (1.6%)	60 (98.4%)

* *This count represents the number of subjects with both a 1-month CT and later follow-up CT, so that a sac diameter change may be evaluated.*

2.4 *PATENCY*

Patency was defined as the absence of complete occlusion (100%) of the device or treated vessel. Thrombosis was defined as complete occlusion (100%) of the device or native vessel. Thrombosis could be either within the device (device thrombosis) or the native vessel outside the device treatment area (vessel thrombosis). Stenosis was defined as narrowing of the blood flow lumen that was less than 100% occlusion. Stenosis could be either within the device (device stenosis) or the native vessel outside the device treatment area (vessel stenosis). Patency, thrombosis, and stenosis may be evidenced by CT, angiography, ultrasound or other imaging modality, or pathological analysis and was assessed by the sites for the study. Patency incidence was calculated as the number of subjects with patency divided by the number of subjects with readable scans.

There were no reported adverse events for patency-related issues among all the subjects implanted.

2.5 MIGRATION

Migration was evaluated by the Independent Core Lab and was defined as evidence of proximal or distal movement of the stent graft >10 mm relative to fixed anatomic landmarks (i.e. superior mesenteric artery) compared to the 1-month CT scan. Migration incidence was calculated as the number of subjects with migration divided by the number of subjects with readable paired scans.

There were no subjects with a device migration, identified by the imaging core laboratory, through 1 year.

2.6 *ENDOLEAKS*

Endoleaks were evaluated by the Independent Core Lab and defined by the persistence of blood flow outside the lumen of the endovascular graft, but within the aneurysm sac as assessed on CT scan.

The Kaplan-Meier methodology was used to estimate freedom-from-endoleak rates across the duration of the study. This accounts for subjects who were lost-to-follow-up or otherwise incapable of providing a contrast CT through 1 year. At 12 months, 61 patients had evaluable imaging for endoleaks. The freedom from Type Ia endoleak rate at 6 months and 1 year was 98.7% at both time points (**Table 27**) as one subject reported a Type Ia endoleak. The Type Ia endoleak was reported at the 1-

month follow-up visit and treated post-operatively on day 48 with a balloon expandable stent. The Type Ia endoleak resolved, and aneurysm expansion was not reported for this subject. This event was adjudicated to be device related.

The freedom from Type II endoleak rate at 6 months and 1 year was 53.3% and 51.7%, respectively. There was only one case of aneurysm sac expansion reported which the CEC adjudicated to be likely due to a Type II endoleak. The subject exited the study without having a AAA secondary intervention.

Due to the high Type II endoleak rate, an analysis was performed on the ELEVATE study to define factors responsible for Type II endoleaks. Baseline demographics, medical history, and anatomical measurements at baseline were evaluated using a logistic regression model. Among all baseline comorbidities, smoking status was a significant negative predictor (protective) for Type II endoleaks (Odds ratio: 0.12, 95% CI 0.026-.602).

The freedom from unknown endoleak rate at 6 months and 1 year was 96.0% and 94.3%, respectively. Unknown endoleaks were not adjudicated by the CEC.

There were no Type Ib, III or IV endoleaks observed in the study through 1-year.

Table 27: Kaplan Meier Estimates of Endoleaks (EL)

Kaplan Meier Estimates	6 Months	12 Months
Freedom from type IA EL	98.7%	98.7%
Freedom from type II EL	53.3%	51.7%
Freedom from unknown type EL	96.0%	94.3%

2.7 Loss of Stent Graft Integrity through 12-Month Follow-up

The integrity of the stent graft was evaluated by the independent imaging core laboratory using abdominal x-rays at regularly scheduled follow-up visits. Any fractured stents, and any other issues compromising the integrity of the stent graft were reported. The discharge or 1-month abdominal x-ray served as the baseline for all evaluations of stent graft integrity. Loss of stent graft integrity incidence was calculated as the number of subjects with loss of stent graft integrity divided by the number of subjects with adequate imaging to assess the endpoint.

The core lab reported no device fractures or other issues compromising the integrity of the stent graft at any time point.

2.8 Thromboembolic Events

Thromboembolic events were defined as deep vein thrombosis, pulmonary embolism, embolic stroke, limb ischemia in the presence of occlusion or thrombosis with the stent graft. There were no thromboembolic events requiring a secondary intervention reported by the sites at any timepoint.

2.9 CONVERSION TO OPEN REPAIR THROUGH 12 MONTHS

The surgical conversion rate through 365 days post-treatment, using the Alto™ device, was 1.3% (1 of 75). There was one surgical conversion > 31 days post procedure. The subject was converted to open repair at 273 days post implant due to stent infection (**Table 28**).

Table 28 – Surgical Conversion through 365 Days

Variable	≤30 Days	31-365 Days	0-365 Days
Conversion	0	1.3% (1/75)	1.3% (1/75)

The Kaplan-Meier estimate of freedom from Surgical Conversion through 365 days was 98.6%. See **Table 29** below.

Table 29: Freedom from Surgical Conversion through 365 Days: Kaplan-Meier Estimate

Variable	Treatment to 30 days	31 to 180 days	181 to 365 days
Number at risk[1]	75	75	73
Number of events[2]	0	0	1
Number censored[3]	0	2	34
Kaplan-Meier estimate[4]	100	100	98.6
Standard error	0	0	1.4

[1] Number of subjects at risk at beginning of interval
[2] All events within the time interval
[3] Subjects are censored on the current post-op day as of the date of the data-cut, having completed the study, or upon exit or loss to follow-up
[4] Estimate at the end of the time interval

2.10 SECONDARY INTERVENTIONS

A total of 3 AAA-related secondary procedures were performed in 2 of 75 subjects (2.7%); one subject had a Type 1A endoleak and received ballooning and bare metal stent placement for intervention on post-operative day 48 which successfully treated the endoleak. This was adjudicated by the CEC to be device and procedure related. Another subject had a device infection and was converted

to open repair on post-operative day 273. This was adjudicated by the CEC to be device related, but not procedure related.

3. *Subgroup Analyses*

The following preoperative characteristics were evaluated for potential association with outcomes with descriptive statistics only: gender.

Men and women both had high rates of treatment success at 1 year. No endpoint failures were seen among the female cohort. There were no notable differences in outcomes between men and women.

4. *Pediatric Extrapolation*

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 52 investigators of which none were full-time or part-time employees of the sponsor and 9 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0 investigators
- Significant payment of other sorts: 9 investigators
- Proprietary interest in the product tested held by the investigator: 0 investigators
- Significant equity interest held by investigator in sponsor of covered study: 0 investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this Panel Track PMA Supplement 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 PRECLNICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The ELEVATE study met its pre-defined primary effectiveness endpoint defined as a composite of peri-procedural technical success and the absence of the following post-operatively through 1 year: type I and III endoleak, stent graft migration, AAA enlargement, AAA rupture, conversion to open repair, occlusion or kink requiring secondary intervention, thromboembolic event attributable to stent graft requiring secondary, and stent fracture requiring secondary intervention.

Of 61 patients evaluated at 1 year, 58 patients had successful aneurysm treatment (95.1%). Peri-procedural technical success was 100% (75 of 75). The events determined to meet the definition of unsuccessful aneurysm treatment included the following: One conversion to open repair (1.3%; 1 of 75) was reported at 273 days post implant, due to device infection; one Type Ia endoleak was reported for one subject in the 30-day window and was treated with a balloon expandable stent; one aneurysm enlargement, attributed to a type II endoleak, was noted at the 1-year follow-up visit. No additional device-related secondary interventions were seen as defined in the endpoint. No stent graft occlusions, migrations, or fractures were reported at any timepoint.

A one-sided Clopper-Pearson 95% confidence interval was constructed for the treatment success rate seen in the study. The lower bound of this confidence interval was compared against the performance goal to evaluate the null hypothesis that the expected treatment success rate was less than or equal to 80%. The null hypothesis was rejected given the lower bound of 90%, thus the data supported the alternative hypothesis that treatment success was greater than 80%.

Given that 14 of 75 subjects were enrolled in the study but lacked the appropriate information to evaluate the primary endpoint, a post-hoc sensitivity analysis was conducted to calculate the Kaplan-Meier estimate of the primary endpoint. The Kaplan-Meier estimate of the primary endpoint shows 96.8% freedom from failure at 1-year, which is comparable to the prespecified primary analysis finding of 95.1%.

Based on the clinical endpoint outcomes presented above, there is reasonable assurance of effectiveness of the Alto™ Abdominal Stent Graft System for the proposed intended use.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory testing, animal studies and data collected in a clinical study to support PMA approval as described above.

Safety outcomes in subjects treated with the Alto™ Abdominal Stent Graft System, through one year, included an all-cause mortality rate of 4.0% (3 of 75), AAA-related mortality rate of 0% (0 of 75), as well as a MAE incidence rate of 5.3% (4 of 75) at 30 days and 10.7% (8 of 75) through 1 year.

These data, observed during the follow-up visits of all subjects through 1-year, demonstrate a reasonable assurance of safety of the Alto™ Abdominal Stent Graft System for the proposed intended use.

C. Benefit/Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. These include:

- Treatment benefits
  - Minimally invasive procedure
  - Reliable device delivery and deployment (100% technical success)
  - Procedure time (90 minutes)
  - Minimal blood loss (52.5 cc)

- Outcome benefits
  - Major adverse events (5.3% through 30 days, 10.7% through 12 months), and no (0%) AAA Mortality
  - No AAA rupture, and 1.6% AAA enlargement
  - No Stent Fractures, no device occlusions, and no device migrations
  - AAA-related secondary intervention rate (2.7%)

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above.

The primary risks of AAA treatment with the Alto™ Abdominal Stent Graft System through 1-year post-treatment include:

- 2.7% Device-related adverse events

- 2.7% AAA-related secondary interventions
- 10.7% Major adverse events
- 4.0% Death (all-cause)

Additional factors to be considered in determining probable risks and benefits for the Alto™ Abdominal Stent Graft System included exclusion of 65 subjects from participation in the ELEVATE study. The 65 excluded subjects were rejected by either: Imaging Services, the CRB, or the Site Investigator, which introduces uncertainty as to whether the risk profile of subjects enrolled in the ELEVATE study was altered as a result of the subject exclusion. This uncertainty was mitigated by incorporating the exclusion criteria used by Imaging Services, the CRB, and the Site Investigators into the Alto™ Abdominal Stent Graft System indications statement and labeling.

In conclusion, given the available information above, the data supports that for the endovascular repair of infrarenal abdominal aortic aneurysms the probable benefits outweigh the probable risks.

1. Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

D. Overall Conclusion

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. The pre-clinical testing performed in accordance with applicable guidance documents and national and international standards confirmed that the Alto™ Abdominal Stent Graft System met its performance and design specifications, thus providing a reasonable assurance of safety and effectiveness of the device.

The results of the clinical study provide reasonable assurance of safety and effectiveness of the Alto™ Abdominal Stent Graft System, to treat patients with AAA. The 30-day, 6 month and 1 year clinical outcomes, 100% technical success rate and the 95.1% treatment success rate, provide evidence that patients are likely to benefit from the use of this device for endovascular repair of infrarenal AAAs.

XIII. CDRH DECISION

CDRH issued an approval order on March 13, 2020. The final conditions of approval cited in the approval order are described below:

You have agreed to provide a Clinical Update to physician users at least annually. At a minimum, this update will include the following regarding the Alto™ Abdominal Stent Graft System:

a. For your Case Selection and Sizing Study described below, a summary of the number of patients for whom data are available, with a summary of the agreement between treating physician and Endologix Imaging Services screening, as well as any adverse events reported.

b. For your Alto™ US and OUS Post-Approval Study described below, a summary of the number of patients for whom data are available, with the rates of major adverse events, aneurysm-related mortality, aneurysm rupture, secondary endovascular procedures, conversions to open surgical repair, endoleaks, aneurysm enlargement, prosthesis migration, occlusions, stenoses, losses of device integrity, and other procedure or device-related events. Reasons for secondary interventions and conversion to open surgery as well as causes of aneurysm-related death and rupture are to be described.

c. Relevant information from commercial experience of the Alto™ Abdominal Stent Graft System within and outside the United States.

d. A summary of any explant analysis findings regarding the Alto™ Abdominal Stent Graft System.

The Clinical Update for physician users and the information supporting the updates must be provided in the Annual Report.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Each report, identified as a PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address identified in the approval order.

1. *Case Selection and Sizing Study:* This is a prospective, consecutively enrolling, single-arm, multi-center study. The study purpose is to ensure the patient population receiving the first commercial implants of the Alto™ device is consistent with the patient population enrolled in the ELEVATE pivotal study and to evaluate differences in the subject screening conducted by treating physicians and the Endologix Imaging Services. The study will prospectively enroll US subjects found to meet the anatomic criteria for Alto™ device implantation as specified in the approved labeling and assessed by treating physicians from a minimum of 15 US institutions who have successfully completed the Alto™ Training Program. Once consented by the institution, the treating physician will record the following per subject, at a minimum:

1) quantitative measurements of the subject's aortic morphology (e.g., aortic diameter, aneurysm neck length, aneurysm neck angulation); 2) commentary regarding the subject's general suitability for endovascular aneurysm repair (EVAR) using the Alto™ device; 3) a recommendation for implantation with the Alto™ device; and, 4) the Alto™ device and component(s) sizes appropriate for treatment, if applicable. The de-identified, diagnostic CT scans associated with each consented subject will then be sent to Endologix Imaging Services, who will independently assess each subjects' suitability for EVAR using the Alto™ device and record the same information as that recorded by the treating physician. At a minimum, the first 100 commercial subjects receiving an implantation recommendation from Endologix Imaging Services will be treated with the Alto™ device. Subjects will be consented until a minimum of 100 subjects have been treated with the Alto™ device. An independent, third-party will evaluate the differences between the data from the treating physicians and Endologix Imaging Services for all consented subjects; at a minimum, a Bland-Altmann method with a 95% confidence interval will be used to provide the expected limits of agreement for quantitative measures (e.g., aortic diameter), percent agreement in the format of a 2x2 contingency table will be used to provide the expected limits of agreement for qualitative measures (e.g., implantation recommendation), and the additional analyses of sensitivity, specificity, and positive and negative predictive values will be calculated for the recommendation for implantation using Endologix Imaging Service as the gold standard. All adverse events resulting in a product complaint occurring in consented subjects within 30 days of an Alto™ implantation procedure will be captured through the Endologix quality system and reported. No clinical follow-up imaging or evaluation(s) will be collected for consented subjects for the purposes of this study. Consented subjects will continue to receive the standard of care as directed by their treating physician outside of this study. Study reports will contain, at a minimum, all currently consented subject and adverse event data, as well as the aforementioned and corresponding analyse(s) conducted by the independent, third party.

2. *Alto™ US and OUS Post Approval Study:* This is a prospective, multi-center, multi-national, post approval study. The objective of the study is to collect confirmatory safety and effectiveness data on the Alto™ Abdominal Stent Graft System for the endovascular treatment of infrarenal abdominal aortic aneurysms in routine clinical practice. Upon completion of the Alto™ Case Selection and Sizing study, this post approval study will begin prospectively enrolling subjects according to clinical guidelines and the treating physician's judgement. Notably, treating physicians will be making the determination regarding whether a subject should be enrolled and treated; they may request input from the Endologix Imaging Services. A minimum of 300 subjects at up to 40 sites in the US and 20 sites from outside the US, with no more than one-third non-US subjects, will be enrolled. Follow-up will occur at 30 days, 6 months, 1 year, and annually thereafter to 5 years. The primary composite endpoint is freedom from aneurysm-related complications, including conversion to open surgery, Type I and III endoleaks, device migration (>10 mm), aneurysm sac enlargement (>5 mm), device- and procedure-related secondary interventions, occlusion, aneurysm rupture, and aneurysm-related death. Adjudication of the

primary composite endpoint will be conducted by an external, independent core lab at annual intervals through 5 years. Additional endpoints will be collected and reported annually through 5 years, including but not limited to the following: individual components of the primary composite endpoint, technical success, major adverse events, secondary interventions, all types of endoleaks, stenoses, losses of device integrity, other procedure- or device-related events, and rate of aneurysm neck expansion, as adjudicated by an independent external core lab. Outcomes will be reported using descriptive statistics. Additionally, a subgroup analysis that stratifies outcomes by subjects with certain vascular morphology will be reported.

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.