DATE: **NOVEMBER 21, 2011**

FROM: **SCIENTIFIC REVIEWER, CDRH/ODE/DCD/PVDB**

SUBJECT: **EVALUATION OF AUTOMATIC CLASS III DESIGNATION PETITION #K102333 AND APTUS ENDOSTAPLING SYSTEM**

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TO: **THE RECORD**

REGULATORY INFORMATION

An endovascular suturing system is intended to provide fixation and sealing between endovascular aortic grafts and the native artery. The device is used in patients whose endovascular grafts have exhibited migration or endoleak, or are at risk of such complications, in whom augmented radial fixation and/or sealing is required to regain or maintain adequate aneurysm exclusion. The device consists of a helical metal endovascular suture (the Endostaple) and implantation means (the Endostaple Applier) as well as a steerable guide sheath (the EndoGuide) for access and delivery within the vasculature. The Endostaples are applied during endovascular graft procedures and affix the proximal end of the graft to the aortic wall.

NEW REGULATION NUMBER: 870.3460 ENDOVASCULAR SUTURING SYSTEM

CLASSIFICATION: II

PRODUCT CODE: OTD

BACKGROUND

K102333 was previously found not substantially equivalent (NSE) due to lack of a valid predicate.

In response to our NSE determination, the sponsor requested an evaluation of Automatic Class III Determination ("de novo") for their device, recommending that their device be reclassified as a Class II device.

The petition for reclassification was subsequently placed on hold, and a De Novo Additional Information (AI) Request was sent.

The sponsor responded to our AI letter. Based upon their response, as well as the additional information subsequently received through interaction, we recommend that this device be reclassified into class II under the criteria for classification set forth in section 513(a)(1) of the FD&C Act.

REVIEW TEAM

The review team and corresponding disciplines for this petition for reclassification is comprised of:

1. Clinical
2. Animal Studies
3. Engineering (implant)
4. Engineering (delivery system), Biocompatibility, Sterility & Shelf-life
5. MR Compatibility
6. RF Heating
7. Signatory

INDICATIONS FOR USE

The Aptus EndoStapling System is intended to provide fixation and sealing between endovascular aortic grafts and the native artery. The Aptus EndoStapling System is indicated for use in patients whose endovascular grafts have exhibited migration or endoleak, or are at risk of such complications, in whom augmented radial fixation and/or sealing is required to regain or maintain adequate aneurysm exclusion.

DEVICE DESCRIPTION

The Aptus EndoStapling System is comprised of an endovascular suture (the EndoStaple) and implantation means (the EndoStaple Applier) as well as a steerable guide sheath (the EndoGuide) for access and delivery within the vasculature. The system is intended to provide fixation and sealing between endovascular aortic grafts and the native artery. This is accomplished via selective catheter placement of discrete helical sutures (EndoStaples) through the endograft and into the tissue of the native vessel (aorta) around the circumference of the endograft. Access to the intended implantation site is gained through the use of the Steerable Endoguide, a deflectable guide sheath. The EndoStaples are implanted, one at a time, by the EndoStaple Applier, a battery-powered, software-controlled, catheter-based device.

Principles of Operation – System

The Steerable EndoGuide is positioned near the end of the endograft and deflected so as to "point" to the desired EndoStaple implant location. EndoStaples are loaded into the EndoStaple Applier from the EndoStaple Cassette by placing the distal end of the EndoStaple Applier catheter into the EndoStaple cassette and pressing the reverse control button on the control handle. The EndoStaple is now retained within the threaded housing and is ready to be implanted. EndoStaple implantation is accomplished in a two-stage process. After the EndoStaple Applier is loaded and positioned at the desired location within the patient's vasculature via the Steerable EndoGuide, pressing the forward control button on the EndoStaple Applier control handle rotates the EndoStaple in the forward direction. The EndoStaple is rotated

and partially driven out of the threaded housing. This is the initial implantation position or "pause position". From the pause position, the EndoStaple implantation process can be completed by pressing the forward button a second time or the EndoStaple can be removed by pressing the reverse button, which rotates the EndoStaple back into the threaded housing. Audible tones and blinking lights during operation indicate the position of the EndoStaple and the available direction of motion. The process is repeated for each EndoStaple to be implanted. Aptus recommends a minimum of four EndoStaples be placed, as evenly distributed as possible around the circumference of the endograft.

Component Descriptions

Steerable EndoGuide with Obturator:

The Aptus Steerable EndoGuide is a sterile, single use, disposable device designed to direct the Aptus EndoStaple Applier to the desired location for EndoStaple implantation. The device is designed for over-the-wire delivery within the patient's vasculature and is compatible with a 0.035" guide wire. The Steerable EndoGuide consists of a 12 Fr (inner diameter) guide sheath with integrated control handle, and a matching 12 Fr obturator. The outer diameter of the EndoGuide guide sheath is approximately 16 Fr. The overall working length of the Steerable EndoGuide is 62 cm.

The Steerable EndoGuide and Obturator are made from industry standard materials as detailed in Table 1 in the Biocompatibility section of this Decision Summary.

All patient-contacting components of the Steerable EndoGuide and Obturator system have met the requirements of ISO 10993 in consideration of the relevant FDA G95-1 guidance.

The Steerable EndoGuide consists of two lumens - the main lumen provides passage for the EndoStaple Applier and the second lumen contains the control cord. The control cord is attached to the distal tip of the Steerable EndoGuide and to a tensioning mechanism contained within the control handle. The distal portion of the Steerable EndoGuide catheter, which is normally straight, can be deflected by applying tension to the control cord. A C-shaped radiopaque marker is located at the distal tip of the Steerable EndoGuide to aid in rotational orientation under fluoroscopy.

The control handle contains the tensioning mechanism and includes a hemostatic seal to minimize blood loss during access and removal of the EndoStaple Applier and Obturator. Deflection of the distal tip of the catheter is accomplished by rotating the Control Knob located on the control handle, which applies tension to the control cord.

The Obturator is used during vessel access and is designed to follow the guide wire and provide atraumatic access through tortuous vasculature. Figure 11-1 illustrates the components of the Steerable EndoGuide and Obturator.

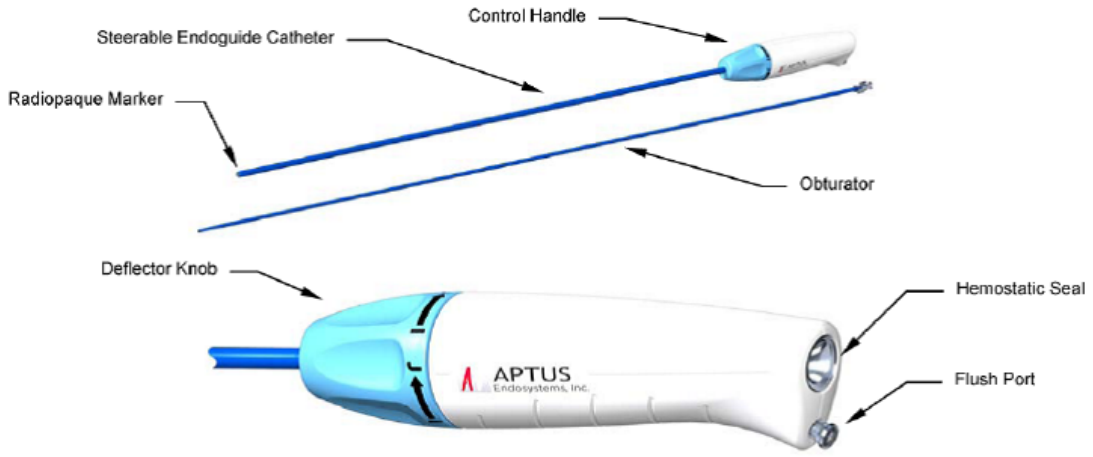


Figure 11-1: Steerable EndoGuide with Obturator

EndoStaple:

The Aptus EndoStaple is an endovascularly-placed suture designed to attach aortic endografts to the native vessel wall. The EndoStaple is manufactured from **[Redacted as (b)(4)]** . The **[Redacted as (b)(4)]** used in the EndoStaple has met the requirements of ISO 10993 in consideration of the relevant FDA G95-1 guidance.

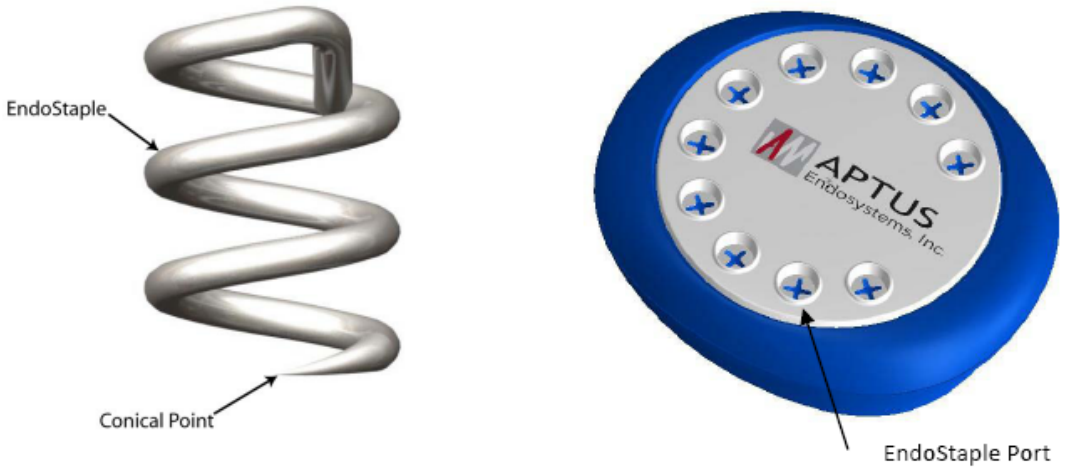
The EndoStaple is approximately 4.5mm in total length and approximately 3.0mm in diameter. The leading end is sharpened to a conical point to act as an integral needle facilitating deployment through the graft material and vessel wall. It is designed to penetrate normal to diffuse calcified tissue up to 2.0mm thick.

The proximal end of the EndoStaple includes a diagonal crossbar, which functions as a suture anchor to prevent over penetration of the EndoStaple. The crossbar further serves to engage with the EndoStaple Applier for loading and implantation. The body of the EndoStaple is helically-shaped allowing the EndoStaple to engage tissue, securing attachment of the endograft to the vessel wall in a fashion similar to that of an interrupted suture, and in contrast to typical endograft hooks or barbs.

Ten (10) EndoStaples are pre-packaged into a cassette, which is supplied sterile to the user. The cassette is designed to facilitate easy and accurate loading of the EndoStaple into the EndoStaple Applier. Figure 11-2(a) illustrates the features of the EndoStaple. Figure 11-2(b) illustrates the EndoStaple Cassette. Figure 11-2 is not to-scale.

Figure 11-2.

(a) EndoStaple **(b) EndoStaple Cassette**



EndoStaple Applier:

The Aptus EndoStaple Applier is a sterile single-patient use disposable device designed to implant one helical EndoStaple at a time. The EndoStaple Applier is designed for use with the Steerable EndoGuide.

The EndoStaple Applier is made from industry standard materials as detailed in Table 1 of the Biocompatibility section of this Decision Summary. All patient-contacting components of the EndoStaple Applier system have met the requirements of ISO 10993 in consideration of the relevant FDA G95-1 guidance.

The EndoStaple Applier is comprised of an 11.8 Fr (outer diameter) catheter and integrated control handle. The single lumen catheter consists of an outer jacket, EndoStaple housing, EndoStaple driver, and flexible drive shaft. The outer jacket is designed to **[Redacted as (b)(4)]** The EndoStaple housing contains **[Redacted as (b)(4)]** and retains the single EndoStaple at the distal tip of the catheter. The driver engages with the diagonal crossbar of the EndoStaple, which is used to rotate the EndoStaple during loading and implantation. The flexible drive shaft connects the driver to the electric motor **[Redacted as (b)(4)].**

The control handle contains a **[Redacted as (b)(4)]**. The controller and firmware control the rotation of the EndoStaple during loading and implantation by monitoring the motor's current and the number of turns of the drive shaft.

Figure 11-3 details the components of the EndoStaple Applier.

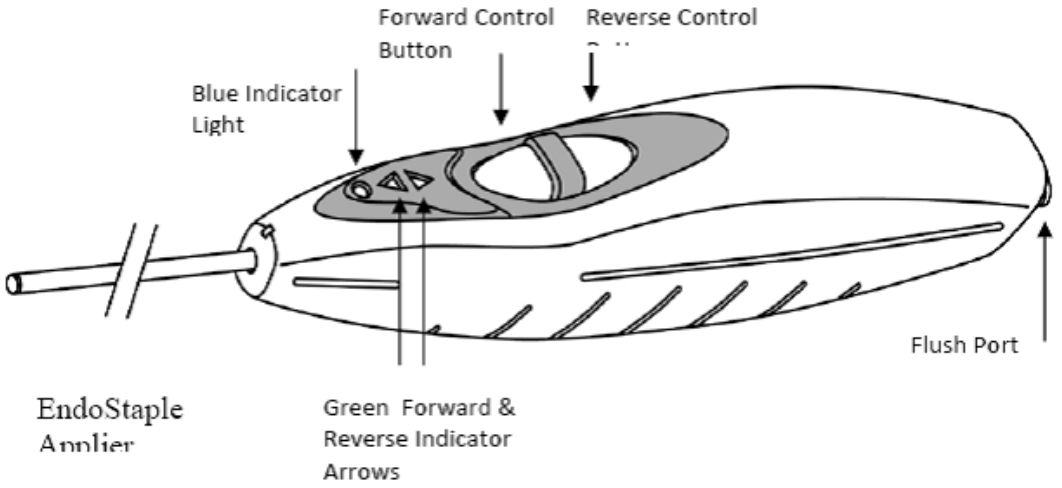


Figure 11-3. EndoStaple Applier

PRECLINICAL/BENCH

BIOCOMPATIBILITY/MATERIALS

The following materials comprise the EndoStapling System:

Table 1: Device Materials

[Table redacted in its entirety pursuant to (b)(4) TS.]

The patient-contacting components of the Aptus EndoStapling System have been evaluated with respect to their intended use per ISO 10993-1:2003. Testing was performed on finished, sterilized devices.

The Steerable EndoGuide, EndoStaple Applier, and EndoStaple implant were evaluated for cytotoxicity (ISO 10993-5), irritation or intracutaneous reactivity and sensitization (ISO 10993-10), systemic toxicity and material-mediated pyrogenicity (ISO 10993-11), and hemocompatibility – hemolysis, thrombosis, and coagulation (ISO 10993-4).

Further, the EndoStaple implant was evaluated for genotoxicity and carcinogenicity/mutagenicity (ISO 10993-3), subacute and subchronic toxicity (ISO 10993-11), and underwent two-and twelve-week implantation studies per ISO 10993-6.

All patient-contacting devices were shown to be biocompatible per ISO 10993-1:2003 with respect to their intended uses.

SHELF LIFE AND STERILITY

The EndoStapling System is packaged as two components – the Steerable EndoGuide with Obturator and the EndoStaple Applier with Cassette (containing 10 EndoStaples). Each device is placed in a **[Redacted as (b)(4)]** tray with lid, which is enclosed in a standard **[Redacted as (b)(4)]** pouch and **[Redacted as (b)(4)]**. The single pouch is placed in an outer carton along with the instructions for use (IFU). Five outer cartons are placed into each shipper box for shipment to/from sterilization and for shipment to customers.

The EndoStapling System is **[Redacted as (b)(4)]**. The sterilization process validation and routing monitoring comply with ISO 11135:2007, using **[Redacted as (b)(4)].**

The shelf life of one year has been established through testing of devices and packaging exposed to a combination of accelerated and real-time aging. Accelerated aging was conducted on packaged product based on standard Arrhenius calculations. In addition, real-time aging on the packaging was separately completed. All test devices and packages underwent environmental and transportation conditioning prior to testing (ASTM D4332 and D4169-09 cycle #13). Product was subjected to visual inspection as well as simulated use and mechanical integrity testing to verify performance. Packaging was subjected to visual inspection followed by bubble and peel testing (ASTM F2096-04 and F88-09).

ANIMAL STUDIES

The animal study sought to evaluate the deployment and performance of the helical staples in attaching an endovascular graft to the aortic wall as well as to validate the radiopacity of the Aptus system. Fourteen (14) calves received the device under heparinization and general anesthesia after suitable periods of acclimation and baseline physical examinations. Radiographic sizing was attained by angiography during deployment while 30, 60, and 150-day sacrifices permitted review of radiologic, gross postmortem, morphometric and histological findings. Findings suggest that the deployment and fixation of the implant appears reasonably safe and that the biologic reaction *in vivo* is acceptable, resulting in good patency and low levels of inflammation.

A cadaver study was also performed to investigate migration resistance of various endovascular grafts with and without EndoStaple use. One investigational endovascular graft and seven commercially-available endovascular grafts were implanted in non-preserved human cadaveric aortas. Various numbers of EndoStaples and hand-sewn sutures were compared following the test methods of ISO 25539-1 §7.3.2.5, with the noted exception of placement in human cadaveric aortas rather than mock aorta tubes. Results demonstrated improved migration resistance by the addition of EndoStaples to the proximal attachment zones of endovascular grafts.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

Electrical safety testing was performed on the EndoStaple Applier per the relevant requirements of IEC 60601-1:1988 + Amendment 1:1991 + Amendment 2:1995 and IEC 60601-1-2:2001 + Amendment 1:2004.

Based on successful completion of the testing, the Aptus EndoStaple Applier is deemed compliant to relevant electrical and electromagnetic safety requirements of IEC 60601-1:1988 + Amendment 1:1991 + Amendment 2:1995 and IEC 60601-1-2:2001 + Amendment 1:2004.

MAGNETIC RESONANCE (MR) COMPATIBILITY

Magnetic Resonance (MR) Compatibility was evaluated with RF heating, MR force, MR torque and image artifact testing. The testing addressed the particular attributes of the device design with respect to the requirements of the following standards:

- Radio Frequency Induced Heating per ASTM F 2182 -02a
- Magnetically Induced Displacement Force per ASTM F 2052 - 02
- Magnetically Induced Torque per ASTM F 2213 -02
- Evaluation of MR Image Artifacts per ASTM F 2119 – 01

This testing represents the MRI verification for implantable endovascular prostheses as specified by ISO 25539-1:2003. Results demonstrate satisfactory MR compatibility of the implant when used under the conditions set forth in the device labeling. The Aptus EndoStaples are determined to be MR Conditional. Minor revisions to the labeling were requested from the MR Compatibility reviewer and all revisions were adequately incorporated.

MECHANICAL SAFETY

Comprehensive bench testing has been successfully completed on the Aptus EndoStapling System. Testing includes simulated use, compatibility, durability and corrosion resistance (for the EndoStaple implant), and mechanical strength testing, as summarized in the table below. Testing was performed on finished, sterile devices that were exposed to environmental and transportation conditioning prior to testing (ASTM D4332 and D4169-09 cycle #13). All devices were shown to meet pre-determined acceptance criteria.

	EndoStaple Implant	**EndoStaple Applier**	**Steerable EndoGuide**
Simulated Use	Performance per IFU	Performance per IFU	Performance per IFU
Mechanical Integrity	Weld joint torque strength	Tensile Strengths Torque Strengths	Tensile Strengths Torque Strengths Tip Stiffness
Functional Testing	Torque to remove from Cassette	Ability to deploy min. no. of EndoStaples	N/A
Corrosion Testing	Breakdown potentials	N/A	N/A
Durability Testing	10-yr simulated loading w/o migration, fracture, or endograft damage	N/A	N/A
MRI Compatibility	Minimal heating, displacement force, torque, and image distortion/artifact	N/A	N/A

A summary of each type of test is given below:

- Simulated use testing was carried out in an anatomical model operated under simulated physiological conditions (nominal blood pressure and temperature) with visualization under x-ray. All necessary steps for preparation, use, and removal of the devices per the IFU were followed. Acceptance criteria included successful performance of the device and the ability to complete the simulated procedure.
- Mechanical integrity and functional testing was carried out using torque and tensile load measurement equipment at ambient (room temperature) conditions. All parameters were required to meet pre-defined specifications.
- Corrosion was assessed via cyclic potentiodynamic polarization testing conducted per ASTM F2129-04. Acceptance criteria included a breakdown potential Eb at least **[Redacted as (b)(4)]** greater than the resting potential Er (Eb-Er ≥ 600mV).
- Accelerated durability testing was conducted by cyclically loading the EndoStaple/endograft interface in the axial direction under worst-case physiological loading conditions. Test conditions were derived from Liffman et al.[1] Testing continued for ≥ 380 million cycles (10-years equivalent) per ISO 25539-1. Acceptance criteria included a lack of migration or fracture of the EndoStaples or endografts, and no EndoStaple-induced endograft damage.

SOFTWARE

The EndoStaple Applier component of the Aptus EndoStapling System utilizes software (firmware) for the control of the motor that drives the loading and implantation of the EndoStaple. The firmware was determined to be of a moderate level of concern per the relevant FDA Guidance ("Guidance for the content of Premarket Submissions for Software Contained in Medical Devices" dated May 2005). According to this guidance, software for a device has a "moderate" level of concern if a failure or latent design flaw in the software could result in minor injury to the patient or operator or if a failure or latent flaw could indirectly result in minor injury to the patient or operator through incorrect or delayed information or through the action of a care provider.

The software (firmware) is proprietary and was developed in concert with the device hardware specifically for the EndoStaple Applier application. It is loaded into the hardware during board manufacture and is not user-adjustable. Software control of the Applier includes a power-on self-test, cycle counter, staple deployment monitoring, and various error detection and mitigation routines. The self-test verifies battery voltage and motor function prior to device use, and does not allow the Applier to function if the self-test fails. The cycle counter limits the device to fifteen (15) complete EndoStaple deployments, after which the Applier will not load additional staples. The software monitors Applier driveshaft rotations and the current draw by the motor to determine staple position and proper staple deployment up to the pause state. In the event that the software detects an error with a staple loaded, it attempts to return the staple to the fully retracted position.

Independent verification and validation of the firmware/hardware combination was successfully completed, reviewed and deemed acceptable.

[1] Liffman K, Lawrence-Brown M, Semmens J, *et al*. Analytical Modeling and Numerical Simulation of Forces in an Endoluminal Graft. *J Endovasc Ther* 8:358-71, 2001.

CLINICAL DATA

The sponsor provided clinical data that identifies key elements supporting clinical use of this new device type. These key elements include but are not limited to the treatment of Type I endoleaks, proximal neck dilatation and endograft migration. The proposed clinical need and indications for use are appropriate.

The Aptus EndoStapling System was evaluated in conjunction with an investigational endovascular graft in patients meeting standard EVAR treatment criteria. The sponsor conducted a prospective, multi-center, single-arm, clinical study which enrolled 155 subjects (145 male, average age 73 years) at 25 centers in the United States under the Investigational Device Exemption number **[Redacted as (b)(4)]**.

A total of 810 EndoStaples (range 2-14, median 5) were implanted in 154 subjects. One of the 155 subjects enrolled did not receive EndoStaple implantation due to a conversion to open surgical repair that was not device-related. EndoStaple implantation took an average of 16.8 minutes (standard deviation 11.8 minutes) with a range of 2-125 minutes. Through one-year follow-up, there were no EndoStaple fractures as observed by the core lab.

Through one year follow-up, no subjects experienced endograft migration, one subject had a Type I endoleak identified by the core lab on routine follow-up scans, and one subject required an intervention to address a Type I endoleak. There were 15 reported device malfunctions - five associated with the Steerable EndoGuide, eight associated with the EndoStaple Applier, and two associated with the EndoStaple Cassette; none of these led to any clinical events or adverse patient sequelae. The clinical data demonstrate that the EndoStapling System is safe and effective when used as a proximal fixation tool.

The lead and clinical reviewer worked interactively with the sponsor to revise the labeling to ensure that it contained all relevant data and information for proper use. No additional concerns remain.

LABELING

The Aptus Endostapling System complies with the labeling requirements under 21 CFR 807.87(e) and prescription device requirements under 21 CFR § 801.109. The device is exempt from having adequate directions for lay use. The device labeling bears the following: “Caution: Federal law restricts this device to sale by or on the order of a physician.”

SUMMARY OF INTERACTIVE REVIEW/CORRESPONDENCE

Interaction with the sponsor has been in the form of emails, teleconferences and formal requests. A formal request was sent in the form of an Additional Information (AI) letter to clarify points regarding bench and clinical testing. Teleconferences and emails addressed labeling concerns such as inclusion of all relevant data, indications for use, compatibility with commercially-available endovascular grafts, patient follow-up and possible adverse events.

RISKS TO HEALTH

The table below identifies the risks that may be associated with an endovascular suturing system intended to provide fixation and sealing between an endovascular graft and the native artery.

Risks to Health and Recommended Mitigation Measures

Identified Risk	Recommended Mitigation Measures
Adverse tissue reaction	Biocompatibility Labeling
Infection	Sterility and Shelf Life Testing
Incompatibility with endograft	Bench testing
Migration or fracture of the endovascular suture	Bench testing Animal testing Clinical evaluation
Imaging Incompatibility	Bench testing Labeling
Electromagnetic incompatibility	Electromagnetic Compatibility Labeling
Electrical safety issues	Electrical Safety Testing Labeling
Corrosion	Bench testing
Improper deployment or inability to deploy	Bench testing Animal testing Clinical evaluation Software validation
Failure to prevent endograft migration or Type I endoleak	Bench testing Clinical evaluation Cadaver testing

SPECIAL CONTROLS

In addition to the general controls of the Food, Drug & Cosmetic Act, the Endovascular Suturing System is subject to the following special controls:

(1) The device should be demonstrated to be biocompatible;

(2) Sterility and shelf life testing should demonstrate the sterility of patient-contacting components and the shelf-life of these components;

(3) Non-clinical and clinical performance testing should demonstrate substantial equivalence in safety and effectiveness, including durability, compatibility, migration resistance, corrosion resistance, and delivery and deployment;

(4) Non-clinical testing should evaluate the compatibility of the device in an MR environment;

(5) Appropriate analysis and non-clinical testing should validate electromagnetic compatibility (EMC) and electrical safety;

(6) The sale, distribution, and use of the device are restricted to prescription use in accordance with 21 CFR 801.109; and

(7) Labeling must bear all information required for the safe and effective use of the device as outlined in 801.109(c), including a detailed summary of the non-clinical and clinical evaluations pertinent to use of the device.

CONCLUSION

The sponsor has provided adequate data to demonstrate safety and effectiveness of the EndoStapling System for its intended use. The special controls outlined above appropriately mitigate the identified risks of an endovascular suturing system.

I recommend that the petition for the Aptus EndoStapling System be granted and that the device be classified under the following:

Product Code: OTD
Device/Product Name: EndoStapling System
Class: II
Regulation: 870.3460

RECOMMENDATION - I recommend that the petition be Granted.