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Endurant Evo International Clinical Trial

Clinical Investigation Plan

Version 7.0

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Sponsor
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Previous versions	
Version 1	12 Dec 2014
Version 2	05 Jan 2015
Version 3	NA *(never implemented or distributed)*
Version 4	NA *(never implemented or distributed)*
Version 5	18 Apr 2016
Version 6	16 Nov 2016

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A SYNOPSIS

Protocol Number	10173339DOC
Title	Endurant Evo International Clinical Trial
Investigational Device	Endurant™ Evo AAA Stent Graft System
Study Design	The Endurant Evo International Clinical Trial is a prospective, multi-center, pre-market, non-randomized, single-arm trial.
Purpose	The purpose of the Endurant Evo International Clinical Trial is to evaluate the safety and effectiveness of the Endurant Evo AAA stent graft system for endovascular treatment of subjects with infrarenal abdominal aortic or aortoiliac aneurysms.
Primary Objective	The primary safety objective is to evaluate the safety of the Endurant Evo AAA stent graft system for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms. Safety will be assessed through the proportion of subjects who have a Major Adverse Events (MAE) reported within 30 days post-implantation. The primary effectiveness objective is to evaluate successful delivery and deployment of the Endurant Evo AAA stent graft system with successful removal of the delivery system during the index procedure.
Secondary Objective	Secondary objectives include descriptive analyses of secondary endpoints as well as acute procedural and clinical utility measures.
Primary Endpoints	**Primary safety endpoint:** The primary safety endpoint is defined as the proportion of subjects experiencing a MAE within 30 days post-implantation. MAEs include the occurrence of any of the following events: • All-cause mortality • Bowel ischemia • Myocardial infarction • Paraplegia • Procedural blood loss ≥1000 cc • Renal failure • Respiratory failure • Stroke **Primary effectiveness endpoint:** Technical success at the index procedure (as assessed intra-operatively) is defined as successful delivery and deployment of the Endurant Evo AAA stent graft system in the planned location and with no unintentional coverage of both internal iliac arteries or any visceral aortic branches and with successful removal of the delivery system.
Secondary Endpoints	The following secondary endpoints will be evaluated: • All cause-mortality within 30, 183, and 365 days • Aneurysm-related mortality within 30, 183, and 365 days • Secondary procedures to correct Type I and III endoleaks within 30, 183 and 365 days • Secondary endovascular procedures within 30, 183 and 365 days • Serious adverse events within 30, 183 and 365 days • Aneurysm rupture within 30, 183 and 365 days • Conversion to open surgery within 30, 183 and 365 days • Major adverse events within 183 and 365 days • Stent graft migration at 12-month follow-up visit (as compared to 1- month imaging) • Aneurysm expansion > 5 mm at 12-month follow-up visit (as compared to 1-month imaging) • All endoleaks based on imaging findings at 1- month, 6-month and

	12- month visits • Stent graft occlusion based on imaging findings through 6 months and 12 months • Device deficiencies based on imaging findings through 6 months and 12- months Secondary endpoints will be assessed at annual follow-up visits until 5 years post-implantation.
[redacted]	[redacted]
Subject Population	Subject population will include subjects diagnosed with an infrarenal abdominal aortic or aortoiliac aneurysm who are considered candidates for endovascular repair, and who meet the Inclusion/Exclusion Criteria for the Endurant Evo International Clinical Trial.
Number of Subjects	Under the Endurant Evo International Clinical Trial protocol, 40 subjects will be enrolled consecutively and assessed per the study's primary endpoint to support regulatory approval. Approximately 30 additional subjects may be enrolled to meet additional geography-specific regulatory requirements. Given the Device Deficiencies (DDs) with SAE potential that have occurred within the Endurant Evo trials (transition stent fracture, partial suprarenal stent detachment, and suprarenal stent fracture), enrollment was terminated with a total enrollment of 69 subjects.
Number of Sites	This trial will be conducted at approximately 10 European sites.
Follow-up Schedule	Subjects will have required follow-up visits at the following time points: 1. 1 month following the index procedure 2. 6 months following the index procedure 3. 12 months following the index procedure 4. Annually until 5 years following the index procedure Given the DDs with SAE potential that have occurred within the Endurant Evo trials, the Data Monitoring Committee (DMC) has made additional imaging surveillance recommendations, beyond the required follow-up in the protocol. The additional imaging surveillance recommendations are provided, under separate cover, in the most recent DMC Surveillance and Management letter that has been provided to each investigational site.

Coordinating Principal Investigators	[redacted]
[redacted]	[redacted] bifurcated stent graft is indicated for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms. The Endurant Evo aorto-uni-iliac (AUI) stent graft is indicated for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms in subjects whose anatomy does not allow the use of a bifurcated stent graft. The Endurant Evo AAA stent graft system is indicated for use in subjects with the following characteristics: • adequate iliac or femoral access that is compatible with vascular access techniques (femoral cutdown or percutaneous), devices, and accessories • proximal neck length of o ≥10 mm and infrarenal neck angulation of ≤60° and suprarenal neck angulation of ≤45°, or o ≥15 mm and infrarenal neck angulation of ≤75° and suprarenal neck angulation of ≤60° • aortic neck diameters with a range of 18 mm to 32 mm • distal fixation lengths of ≥20 mm • iliac diameters with a range of 7 mm to 25 mm • morphology suitable for aneurysm repair **Note:** Proximal neck length refers to minimum seal zone.
Inclusion Criteria	Candidates for the Endurant Evo International Clinical trial must be appropriate subjects for endovascular repair of infrarenal abdominal aortic aneurysms or aortoiliac aneurysms (evidenced by screening contrast-enhanced CT or MRA) and have to fulfill all of the following inclusion criteria to be eligible for enrollment in the study: 1) Subject is ≥ 18 years old 2) Subject understands and voluntarily has signed and dated the Informed Consent approved by the Sponsor and by the Ethics Committee/Institutional Review Board. 3) Subject is able and willing to comply with the protocol and to adhere to the follow-up requirements 4) Subject is a suitable candidate for elective surgical repair of AAA as evaluated by American Society of Anesthesiologists (ASA) Physical Status Classification System I, II, or III 5) Subject has an infrarenal abdominal aortic or aortoiliac aneurysm characterized by one or more of the following: a) Aneurysm is > 5 cm in diameter (diameter measured is perpendicular to the line of flow) b) Aneurysm is 4 – 5 cm in diameter and has increased in size ≥ 0.5 cm within the previous 6 months 6) Subject meets all the following anatomical criteria as demonstrated on contrast-enhanced CT or MRA imaging: a) Proximal neck length of ≥ 10 mm with ≤ 60° infrarenal and ≤ 45° suprarenal neck angulation or Proximal neck length of ≥

	15 mm with ≤ 75° infrarenal and ≤ 60° suprarenal neck angulation b) Subject has vascular dimensions, e.g., aortic and iliac diameters, lengths from renal arteries to iliac bifurcation and hypogastric arteries, in the range of sizes available for the Endurant Evo AAA stent graft system (measured intima to intima) and within the sizing recommendations (refer to Endurant Evo AAA stent graft system Instructions for Use (IFU)) c) Subject has a proximal aortic neck diameter ≥18 mm and ≤32 mm d) The distal fixation center of the iliac arteries must have a diameter ≥7 mm and ≤ 25 mm bilaterally for the bifur and unilaterally for the AUI e) Subject has documented imaging evidence of at least one patent iliac and one femoral artery, or can tolerate a vascular conduit that allows introduction of the Endurant Evo AAA stent graft system f) Subject has distal non-aneurysmal iliac (cylindrical) fixation length ≥ 20 mm bilaterally for the bifur and unilaterally for the AUI
Exclusion Criteria	Candidates who meet any of the following exclusion criteria will not be eligible for enrollment in the study: 1) Subject has a life expectancy ≤ 1 year 2) Subject is participating in another investigational drug or device study which would interfere with the endpoints and follow-ups of this study 3) Subject is pregnant 4) Subject has an aneurysm that is: a) Suprarenal/ pararenal/juxtarenal b) Isolated ilio-femoral c) Mycotic d) Inflammatory e) Pseudoaneurysm f) Dissecting g) Ruptured h) Leaking but not ruptured 5) Subject requires emergent aneurysm treatment 6) Subject has a known, untreated thoracic aneurysm >4.5 cm in diameter at time of screening 7) Subject has been previously treated for an abdominal aortic aneurysm 8) Subject has a history of bleeding diathesis or coagulopathy 9) Subject has had or plans to have an unrelated major surgical or interventional procedure within 1 month before or after implantation of the Endurant Evo AAA stent graft 10) Subject has had a myocardial infarction (MI) or cerebral vascular accident (CVA) within 3 months prior to implantation of the Endurant Evo AAA stent graft 11) Subject has a conical neck defined as a >4 mm distal increase from the lowest renal artery over a 10 mm length 12) Subject has a known allergy or intolerance to the device materials 13) Subject has a known hypersensitivity or contraindication to anticoagulants, antiplatelets, or contrast media, which is not amenable to pre-treatment 14) Subject has significant aortic thrombus and/or calcification at either the proximal or distal attachment centers that would compromise fixation and seal of the device at the discretion of the investigator 15) Subject has ectatic iliac arteries requiring bilateral exclusion of hypogastric blood flow

	16) Subject whose arterial access site is not anticipated to accommodate the diameter of the Endurant Evo AAA delivery system (13F-17F) due to vessel size, calcification, or tortuosity 17) Subject is morbidly obese or has other documented clinical conditions that severely inhibit radiographic visualization of the aorta at the discretion of the investigator 18) Subject has active infection at the time of the index procedure documented by e.g. pain, fever, drainage, positive culture and/or leukocytosis considered to be clinically significant per investigator discretion 19) Subject has congenital degenerative collagen disease, e.g., Marfan's Syndrome 20) Subject has a creatinine level >2.00 mg/dl (or >176.8 µmol/L) 21) Subject is on dialysis
Data oversight	A Data Monitoring Committee, Clinical Events Committee, and imaging core lab will be established to independently evaluate subject health status, device performance, and identify any safety concerns regarding subjects' well-being. Contact details of the committees and the core lab will be available in the investigational site file.

B GENERAL INFORMATION

B.1 Introduction

Background

Abdominal aortic aneurysms (AAA) occur in approximately 5% of the general population as estimated by a systematic literature survey of 56 epidemiological studies.[1] This estimate is similar to that observed in an autopsy report from Malmo Sweden, where AAA were found in 4.7% of men and 1.2% of women between 65 and 74 years of age.[2] The prevalence is greater in males (6.0%) compared with females (1.6%) and aneurysms are found more frequently in western countries than in Asia. Risk factors for AAA include advanced age, smoking, family history of AAA, hypertension, atherosclerosis, and hyperlipidemia. The female gender and diabetes were associated with a lower prevalence of AAA.[3]

Aneurysms are prophylactically treated to prevent premature death from rupture. More than one-third of patients with ruptured aneurysms succumb from the event; a proportion that has not decreased appreciably over the last several decades.[4] By contrast, elective treatment of AAA prior to rupture is associated with a perioperative mortality rate below 3%. For this reason, AAA are best managed electively, prior to rupture. Screening tests are recommended in patients at risk for AAA, usually with an abdominal ultrasound imaging study. When an AAA is identified, the clinician's decision to repair the aneurysm rests on assessing the risk of rupture compared with the risk of the repair procedure itself. In this regard, the diameter of the AAA is the only consistent predictor of rupture. As such, patients with AAA greater than 50 mm in diameter are usually recommended for treatment while observation with regular imaging studies is advisable for those with smaller aneurysms.[5] The size threshold is reduced in women, since the normal aorta is smaller in the female gender. The presence of symptoms from an aneurysm, rapid enlargement of the aneurysm, saccular aneurysm configuration, or the distal embolization of aneurysm contents are each considered indications for repair, irrespective of sac diameter. Lastly, a saccular aneurysm configuration is thought to be more prone to rupture and the threshold for AAA repair is lowered when saccular morphology is encountered[6].

There are two general methods for repair of an AAA; traditional open surgical repair and endovascular repair. Traditional open surgical repair has been the standard technique for over six decades.[7,8] Open repair is performed through a transperitoneal or retroperitoneal incision; sewing a prosthetic graft to the aorta above and below the aneurysm. While durable, open repair is associated with a significant risk of perioperative complications. The risk is particularly high in the elderly and in those with multiple medical comorbidities; the population who characteristically develop AAA. The Lifeline registry documented postoperative respiratory failure in 4.3%, myocardial infarction in 4.0%, and renal failure in 2.5% within 30 days of open surgical AAA repair.[9] Endovascular aneurysm repair (EVAR) is the second general technique for aneurysm repair, first described by Volodos in 1986[10] and first successfully performed by Parodi in 1990.[11] The objective of EVAR is to repair the aneurysm through the trans-vascular insertion of an endograft. EVAR has been shown to reduce 30-day and in-hospital mortality, blood transfusions, mechanical ventilation, and ICU and hospital length of stay compared to open surgery.[12] Current endografts, while much improved over earlier devices, still suffer from some shortcomings. Many of the shortcomings of prior designs have been remediated with more durable materials, better stent architecture, and improved manufacturing processes. However, hostile proximal neck anatomies and poor quality access vessels still exclude EVAR as an option for many patients. Anatomical characteristics such as limited proximal aortic neck lengths, severe infrarenal neck angulation, and narrow, tortuous and/or calcified iliac arteries have been identified as risk factors that can limit EVAR success rates and are associated with increased rates of secondary interventions.[13-18] Complications associated with hostile proximal neck anatomy include type I endoleaks and graft migration.[14] Challenging iliac access vessels can hinder placement accuracy resulting in inadequate distal seal zones[16]. Access related complications remain a common cause for conversion to open surgery.[14]

Newer devices must address these previous endograft shortcomings if the applicability and the durability of endovascular repair are to be improved. Engineering of newer device iterations must address interactions between design elements. For instance, lowering the profile of a device with newer sutures, fabrics, stents and assembly methods must also consider the effect such changes will have on one another; both during deployment as well as over long-term follow-up.

Medtronic's next generation AAA stent graft system on the Endurant product platform is the Endurant™ Evo Abdominal Aortic Aneurysm (AAA) stent graft system. The Endurant Evo AAA

stent graft system was designed to further expand EVAR applicability and improve access in patients with challenging anatomies. Key design targets for Endurant Evo include the following:

- Introduction of a lower profile delivery system to allow treatment of patients with challenging anatomies, expand overall patient applicability, and improve procedural ease of use of the system.
- Graft flexibility and limb design optimization to improve conformability in challenging anatomies.
- Introduction of a 3-piece modular system (similar to Endurant IIs), which is engineered to help with placement accuracy by allowing bilateral device length adjustment during deployment and also aids the physicians in better inventory management.
- Enhanced delivery system ergonomic features to improve ease of use.

These enhancements were incorporated in the Endurant Evo AAA stent graft design with an expressed focus on maintaining the high durability and high performance standards established previously in the Endurant family. Scientific literature discussing the clinical performance of the Endurant/Endurant II device documents excellent early and late results. The relatively low rate of device-related complications has the potential to be reduced further with incremental design modifications. Based on the existing scientific literature on Endurant/ Endurant II three primary areas of design change of the Endurant Evo AAA stent graft system cannot be fully evaluated; lower profile, helical limb stent graft optimization, delivery system enhancements.

While these performance/design features are well understood technically and have been comprehensively analyzed/tested through preclinical testing (bench and animal), residual risks associated with the overall performance of the Endurant Evo AAA stent graft system will be confirmed in a clinical investigation designed to evaluate system performance. Therefore, the Endurant Evo International Clinical Trial was designed to evaluate the safety and effectiveness of the device in subjects who are candidates for endovascular repair of infrarenal AAA or aortoiliac aneurysms. Trial endpoints are described in more detail in Section C 2.
Literature review and pre-clinical testing will be provided in the Investigator's Brochure.

B.2 Device Information

B.2.1 Device Description

The Endurant Evo Abdominal Aortic Aneurysm (AAA) stent graft system (manufactured by Medtronic, Inc) is designed for the endovascular repair of infrarenal abdominal aortic or aortoiliac aneurysms. When implanted within the target lesion, the stent graft provides a permanent, alternative conduit for blood flow within the subject's vasculature by excluding the lesion from blood flow and pressure. The stent graft system is comprised of the implantable stent graft and the disposable delivery system. The stent graft is preloaded into the delivery system, which is inserted endoluminally via the femoral or iliac artery and tracked through the subject's vasculature to deliver the stent graft to the target site. Upon deployment, the stent graft self-expands to conform to the shape and size of the seal zones above and below the aneurysm.
The Endurant Evo AAA stent graft system is comprised of two primary components: the Endurant Evo stent graft and the Endurant Evo delivery system. All components of the Endurant Evo AAA stent graft system are pre-market and considered to be investigational.

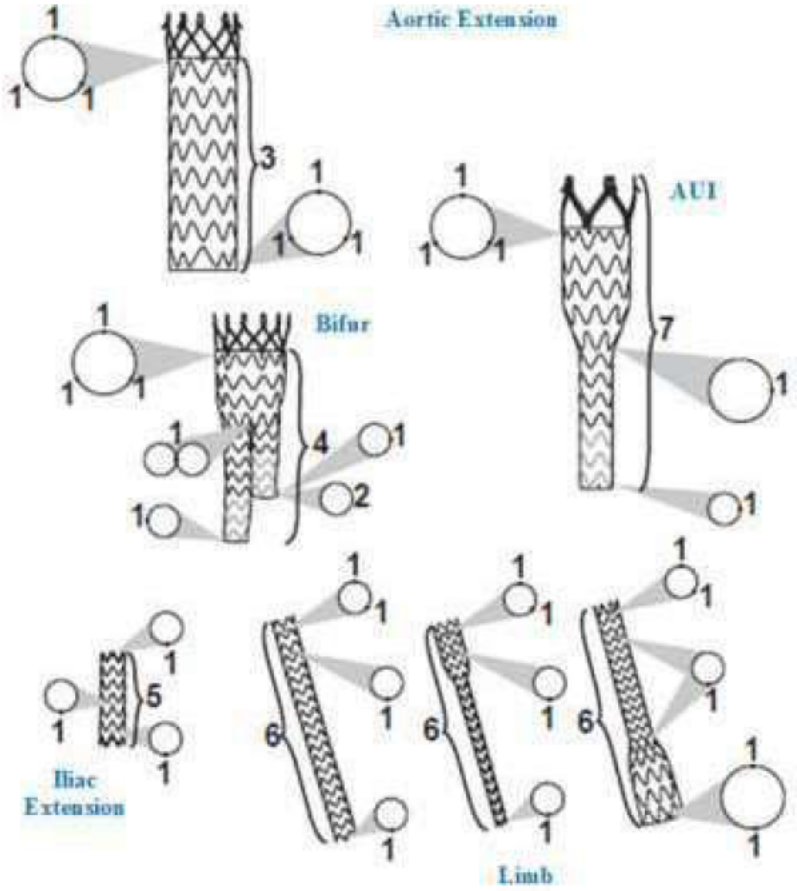
Endurant Evo Stent Graft
The Endurant Evo stent graft is comprised of the following stent graft configurations:

- Bifurcated component
- Limb component
- Aorto-Uni-Iliac (AUI)
- Aortic extensions
- Iliac extensions

Each stent graft component is introduced separately into the vessel and is mated in vivo to the components already in situ. All components are constructed by sewing the self-expanding nitinol stents to a fabric graft. The suprarenal stents with anchor pins on the proximal end of the bifurcated component, the AUI component and the aortic extension are laser cut from a nitinol tube and all other stents are wire-formed. The stents are formed in a ring with opposing ends being terminated together in crimp sleeves. The suprarenal and wire formed stents are sewn to the polyester (PET) graft fabric using ultra high molecular weight polyethylene (UHMWPE) suture.

The graft fabric is [redacted] then cut and seamed into the stent graft component form with PET suture and UHMWPE suture. [redacted].

Radiopaque (RO) markers are sewn onto each component of the stent graft to aid in fluoroscopic visualization and to facilitate accurate placement of each component. Endurant Evo uses three types of radiopaque markers: fold-over ("Clip") markers, tube markers, and coil markers. Clip markers are thin pieces of platinum iridium that are folded over the edge of the graft material in order to show exact location of the fabric edge. Tube markers are sectioned pieces of platinum iridium tubing. Coil marker is a coiled Platinum-Iridium wire which outlines the contralateral gate to facilitate gate cannulation. RO markers are located at the proximal and distal ends of each stent graft component, as well as at the bifurcation of the bifurcated stent grafts to help visualize the edges and locations of the stent grafts, indicate overlap distance between mating stent graft components, and indicate orientation of the contralateral gate on the bifurcated stent graft. RO markers are sewn to the graft fabric using UHMWPE suture to optimize both strength and profile. The nitinol stents may also be visualized under fluoroscopy. The Endurant Evo stent graft configurations are shown in Figure 1 below.



1-RO Marker
2-RO Gate Marker
3-Aortic Extension Configuration
4-Aortic Bifurcated Configuration
5-Limb Configuration
6-Iliac Extension Configuration
7-Aorto-Uni-Iliac Configuration

Figure 1: Endurant Evo Stent Graft Configurations

Endurant Evo Delivery System

The Endurant Evo delivery system is a single use, disposable catheter with an integrated handle designed to provide the user with accurate and controlled deployment. The catheter assembly is flexible and compatible with a 0.035" guidewire.

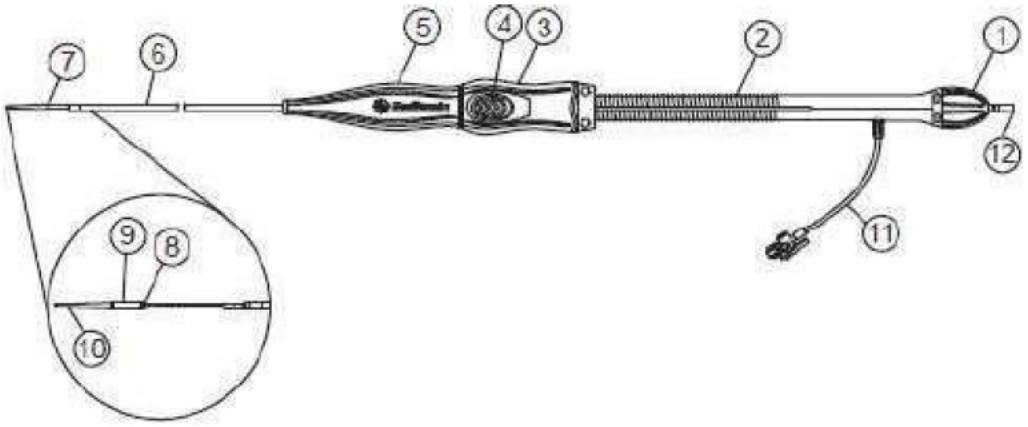
There are two kinds of Endurant Evo delivery systems:

a. Aortic delivery system, which is used to deliver the bifurcated, AUI, and aortic extension components.

b. The Iliac delivery system, which is used to deliver the limb and iliac extension components.

Aortic Delivery System

The working length of the aortic delivery system is 57 ± 2cm. The aortic delivery system is constructed of four concentric single lumen shafts (an outer polymer graft cover with a hydrophilic coating, a heat shrink covered laser cut stainless steel spindle-tube shaft, a polymer middle member shaft, and a nitinol guidewire tube lumen inner member). [redacted]. The aortic delivery system is used to deliver the bifurcated, AUI, and aortic extension stent graft components. Figure 2 provides a pictorial reference of the Endurant Evo aortic delivery system.



1. Rear Grip
2. Screw Gear
3. Retractor Handle
4. Retractor Trigger
5. Front Grip
6. Graft Cover
7. RO Marker
8. Spindle
9. Sleeve
10. Tapered Tip
11. Sideport Extension
12. Rear Luer

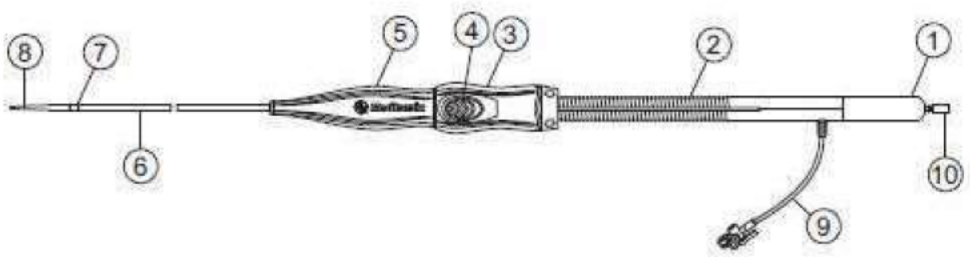
Figure 2: Endurant Evo Aortic Delivery System

The atraumatic polymeric aortic tapered tip is overmolded on the distal end of the nitinol guidewire tube to facilitate tracking through tortuous and calcified vessels. Attached to the proximal end of the tapered tip is a metallic sleeve that holds the suprarenal stent constrained on the spindle. The spindle is a polyether ether ketone (PEEK) overmold on the distal end of the spindle-tube to hold the proximal end of the suprarenal stent axially stationary before release. The aortic tapered tip, [redacted], and the distal end of the graft cover are radiopaque and aid in fluoroscopic visualization. Hemostasis is maintained by the seals within the delivery system that are designed to help minimize blood loss during the procedure. Retraction of the graft cover while the suprarenal stent is held by the spindle and sleeve allows for accurate positioning and deployment of the body of the stent graft components.

Iliac Delivery System

The working length of the iliac delivery system is 57 ± 2cm. The Endurant Evo iliac delivery system (Figure 3) is constructed of four concentric single lumen shafts (an outer polymer graft cover with a hydrophilic coating, a polymer middle member shaft, [redacted], and a PEEK guidewire tube inner lumen). [redacted]. A polymeric, atraumatic tapered tip is overmolded at the distal end of the PEEK guidewire tube lumen to facilitate tracking through tortuous and calcified vessels. The tapered tip, [redacted], and

the distal end of the graft cover are radiopaque and aid in fluoroscopic visualization. Hemostasis is maintained by seals within the delivery system that are designed to minimize blood loss during the procedure. The deployment of the self-expanding stent graft components is facilitated by the retraction of the graft cover.



1. Rear Grip
2. Screw Gear
3. Retractor Handle
4. Retractor Trigger
5. Front Grip
6. Graft Cover
7. RO Tip
8. Tapered Tip
9. Sideport Extension
10. Rear Luer

Figure 3: Endurant Evo Iliac Delivery System

The Endurant Evo AAA stent graft system model numbers are listed in Table B-1.

Table B-1: Device model numbers

Customer acing Number (a.k.a. CFN or REF)	Stent Graft Proximal Diameter (mm)	Stent Graft Distal Diameter1 (mm)	Stent Graft Distal Diameter2 (mm)	Stent Graft Length (Covered) (mm)	Stent Graft Length (Total) (mm)	Catheter Crossing Profile (F)	Device Type (Bifur, Cuff, etc.)
EVBF2213C103CE	22	13	13	103	122	15	Bifurcated Stent Graft
EVBF2213C131CE	22	13	13	131	150	15	Bifurcated Stent Graft
EVBF2513C103CE	25	13	13	103	122	15	Bifurcated Stent Graft
EVBF2513C131CE	25	13	13	131	150	15	Bifurcated Stent Graft
EVBF2813C103CE	28	13	13	103	122	15	Bifurcated Stent Graft
EVBF2813C131CE	28	13	13	131	150	15	Bifurcated Stent Graft
EVBF3213C103CE	32	13	13	103	122	17	Bifurcated Stent Graft
EVBF3213C131CE	32	13	13	131	150	17	Bifurcated Stent Graft
EVBF3613C103CE	36	13	13	103	122	17	Bifurcated Stent Graft
EVBF3613C131CE	36	13	13	131	150	17	Bifurcated Stent Graft
EVUF2213C106CE	22	13	N/A	106	125	15	Aorto-Uni- Iliac Stent Graft
EVUF2213C134CE	22	13	N/A	134	153	15	Aorto-Uni- Iliac Stent Graft
EVUF2513C106CE	25	13	N/A	106	125	15	Aorto-Uni- Iliac Stent Graft
EVUF2513C134CE	25	13	N/A	134	153	15	Aorto-Uni- Iliac Stent Graft
EVUF2813C106CE	28	13	N/A	106	125	15	Aorto-Uni- Iliac Stent Graft
EVUF2813C134CE	28	13	N/A	134	153	15	Aorto-Uni- Iliac Stent Graft
EVUF3213C106CE	32	13	N/A	106	125	17	Aorto-Uni- Iliac Stent Graft
EVUF3213C134CE	32	13	N/A	134	153	17	Aorto-Uni- Iliac Stent Graft
EVUF3613C106CE	36	13	N/A	106	125	17	Aorto-Uni- Iliac Stent Graft
EVUF3613C134CE	36	13	N/A	134	153	17	Aorto-Uni- Iliac Stent Graft
EVCF2222C40CE	22	22	N/A	40	59	15	Aortic Extension Stent Graft
EVCF2222C80CE	22	22	N/A	80	99	15	Aortic Extension Stent Graft
EVCF2525C40CE	25	25	N/A	40	59	15	Aortic Extension Stent Graft
EVCF2525C80CE	25	25	N/A	80	99	15	Aortic Extension Stent Graft
EVCF2828C40CE	28	28	N/A	40	59	15	Aortic Extension Stent Graft
EVCF2828C80CE	28	28	N/A	80	99	15	Aortic Extension Stent Graft
EVCF3232C40CE	32	32	N/A	40	59	17	Aortic Extension Stent Graft
EVCF3232C80CE	32	32	N/A	80	99	17	Aortic Extension Stent Graft
EVCF3636C40CE	36	36	N/A	40	59	17	Aortic Extension Stent Graft
EVCF3636C80CE	36	36	N/A	80	99	17	Aortic Extension Stent Graft

EVEW0808W54CE	8	8	N/A	54	N/A	13	Iliac Extension Stent Graft
EVEW1010W54CE	10	10	N/A	54	N/A	13	Iliac Extension Stent Graft
EVEW1212W54CE	12	12	N/A	54	N/A	13	Iliac Extension Stent Graft
EVEW1414W54CE	14	14	N/A	54	N/A	13	Iliac Extension Stent Graft
EVLW1408W80CE	14	8	N/A	80	N/A	13	Limb Stent Graft
EVLW1408W120CE	14	8	N/A	120	N/A	13	Limb Stent Graft
EVLW1408W160CE	14	8	N/A	160	N/A	13	Limb Stent Graft
EVLW1408W200CE	14	8	N/A	200	N/A	13	Limb Stent Graft
EVLW1410W80CE	14	10	N/A	80	N/A	13	Limb Stent Graft
EVLW1410W120CE	14	10	N/A	120	N/A	13	Limb Stent Graft
EVLW1410W160CE	14	10	N/A	160	N/A	13	Limb Stent Graft
EVLW1410W200CE	14	10	N/A	200	N/A	13	Limb Stent Graft
EVLW1412W80CE	14	12	N/A	80	N/A	13	Limb Stent Graft
EVLW1412W120CE	14	12	N/A	120	N/A	13	Limb Stent Graft
EVLW1412W160CE	14	12	N/A	160	N/A	13	Limb Stent Graft
EVLW1412W200CE	14	12	N/A	200	N/A	13	Limb Stent Graft
EVLW1414W80CE	14	14	N/A	80	N/A	13	Limb Stent Graft
EVLW1414W120CE	14	14	N/A	120	N/A	13	Limb Stent Graft
EVLW1414W160CE	14	14	N/A	160	N/A	13	Limb Stent Graft
EVLW1414W200CE	14	14	N/A	200	N/A	13	Limb Stent Graft
EVLW1416C80CE	14	16	N/A	80	N/A	13	Limb Stent Graft
EVLW1416C120CE	14	16	N/A	120	N/A	13	Limb Stent Graft
EVLW1416C160CE	14	16	N/A	160	N/A	13	Limb Stent Graft
EVLW1416C200CE	14	16	N/A	200	N/A	13	Limb Stent Graft
EVLW1419C80CE	14	19	N/A	80	N/A	15	Limb Stent Graft
EVLW1419C120CE	14	19	N/A	120	N/A	15	Limb Stent Graft
EVLW1419C160CE	14	19	N/A	160	N/A	15	Limb Stent Graft
EVLW1419C200CE	14	19	N/A	200	N/A	15	Limb Stent Graft
EVLW1422C80CE	14	22	N/A	80	N/A	15	Limb Stent Graft
EVLW1422C120CE	14	22	N/A	120	N/A	15	Limb Stent Graft
EVLW1422C160CE	14	22	N/A	160	N/A	15	Limb Stent Graft
EVLW1422C200CE	14	22	N/A	200	N/A	15	Limb Stent Graft
EVLW1425C80CE	14	25	N/A	80	N/A	15	Limb Stent Graft
EVLW1425C120CE	14	25	N/A	120	N/A	15	Limb Stent Graft
EVLW1425C160CE	14	25	N/A	160	N/A	15	Limb Stent Graft
EVLW1425C200CE	14	25	N/A	200	N/A	15	Limb Stent Graft
EVLW1428C80CE	14	28	N/A	80	N/A	16	Limb Stent Graft
EVLW1428C120CE	14	28	N/A	120	N/A	16	Limb Stent Graft
EVLW1428C160CE	14	28	N/A	160	N/A	16	Limb Stent Graft
EVLW1428C200CE	14	28	N/A	200	N/A	16	Limb Stent Graft

The Endurant Evo AAA stent graft system is an investigational class III device in all geographies and is labeled with all the required statements per geography:

- Europe: "Exclusively for clinical investigations" (including translations into local languages)

The use of the Endurant Evo AAA stent graft system is limited to this clinical investigation and has to be done according to the clinical investigational plan and the Instructions for Use (IFU). Required Investigator training for the use of the Endurant Evo AAA stent graft system is described in Section E.4.

B.2.2 Indications for Use

The Endurant Evo bifurcated stent graft is indicated for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms. The Endurant Evo aorto-uni-iliac (AUI) stent graft is indicated for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms in subjects whose anatomy does not allow the use of a bifurcated stent graft. The Endurant Evo AAA stent graft system is indicated for use in subjects with the following characteristics:

- adequate iliac or femoral access that is compatible with vascular access techniques (femoral cutdown or percutaneous), devices, and accessories
- proximal neck length of
  - ≥10 mm and infrarenal neck angulation of ≤60° and suprarenal neck angulation of ≤45°, or
  - ≥15 mm and infrarenal neck angulation of ≤75° and suprarenal neck angulation of≤60°
- aortic neck diameters with a range of 18 mm to 32 mm

- distal fixation lengths of ≥20 mm
- iliac diameters with a range of 7 mm to 25 mm
- morphology suitable for aneurysm repair

Note: Proximal neck length refers to minimum seal zone.

C STUDY PLAN

C.1 Study objectives

The purpose of the Endurant Evo International Clinical Trial is to evaluate the safety and effectiveness of the Endurant Evo AAA stent graft system for endovascular treatment of subjects with infrarenal abdominal aortic or aortoiliac aneurysms..

C.1.1 Primary objectives

The primary safety objective is to evaluate the safety of the Endurant Evo AAA Stent graft system for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms. Safety will be assessed through the proportion of subjects who have a Major Adverse Events (MAE) reported within 30-days post-implantation.
The primary effectiveness objective is to evaluate successful delivery and deployment of the Endurant Evo AAA Stent graft system with successful removal of the delivery system during the index procedure.
(See section *C.2.1 Primary Endpoints* for a detailed description of the evaluation criteria used to assess Primary Objectives)

C.1.2 Secondary objectives

Secondary objectives include descriptive analyses of secondary endpoints as well as acute procedural and clinical utility measures.
(See section *C.2.2 Secondary Endpoints* for a detailed description of the evaluation criteria used to assess Secondary Objectives)

C.2 Clinical Endpoints

C.2.1 Primary Endpoints

C.2.1.1 Primary Safety Endpoint

The primary safety endpoint is defined as the proportion of subjects experiencing a MAE within 30 days post-implantation. MAEs include the occurrence of any of the following events:

- All-cause mortality
- Bowel ischemia
- Myocardial infarction
- Paraplegia
- Procedural blood loss ≥1000 cc
- Renal failure
- Respiratory failure
- Stroke

Detailed definitions of MAEs are provided in Appendix L.2.

C.2.1.2 PrimaryEffectiveness Endpoint

Technical success at the index procedure (as assessed intra-operatively) is defined as successful delivery and deployment of the Endurant Evo AAA Stent graft system in the planned location and with no unintentional coverage of both internal iliac arteries or any visceral aortic branches and with successful removal of the delivery system

C.2.2 Secondary Endpoints

The following secondary endpoints will be evaluated:

- All cause-mortality within 30, 183, and 365 days
- Aneurysm-related mortality within 30, 183, and 365 days
- Secondary procedures to correct Type I and III endoleaks within 30, 183 and 365 days
- Secondary endovascular procedures within 30, 183 and 365 days
- Serious adverse events within 30, 183 and 365 days
- Aneurysm rupture within 30, 183 and 365 days
- Conversion to open surgery within 30, 183 and 365 days
- Major adverse events within 183 and 365 days
- Stent graft migration at 12-month follow-up visit (as compared to 1-month imaging)
- Aneurysm expansion > 5 mm at 12-month follow-up visit (as compared to 1-month imaging)
- All endoleaks based on imaging findings at 1- month, 6-month and 12-month visits
- Stent graft occlusion based on imaging findings through 6 months and 12 months

Device deficiencies based on imaging findings through 6 months and12 months Secondary endpoints will be assessed at annual follow-up visits until 5 years post-implantation Detailed definitions for secondary endpoints are provided in Appendix L.2.

C.3 Study Hypothesis

The Endurant Evo International Clinical Trial is not hypothesis driven; all endpoints will be analyzed descriptively.

Endurant Evo is a next generation abdominal low profile stent graft system on the Endurant product platform. The safety and performance of the commercially available Endurant and Endurant II devices have been well established. As such, this trial is not designed to make a statistical comparison, but rather to collect data demonstrating that the Endurant Evo system performs as expected clinically.

C.4 Study population

The study population will include those subjects who are appropriate candidates for endovascular repair of infrarenal abdominal aortic or aortoiliac aneurysms, and who meet the Inclusion/Exclusion criteria (defined in Section D).

C.5 Study design

The Endurant Evo International Clinical Trial is a prospective multi-center, pre-market, non-randomized, single-arm trial. The trial is designed to assess the clinical safety and performance of the Endurant Evo AAA stent graft system. A sample of 40 subjects will be enrolled consecutively and evaluated at the 30-day primary safety endpoint. Data from these 40 subjects will be analyzed and used to support regulatory approval. All subjects enrolled will continue to be followed under this investigational protocol beyond the 30-day primary endpoint until 5 years post-implantation.

Given the DDs with SAE potential that have occurred within the Endurant Evo trials (transition stent fracture, partial suprarenal stent detachment, and suprarenal stent fracture), enrollment was terminated with a total enrollment of 69 subjects.

Subjects will have required follow-up evaluations at the following time points:

- 1 month following the index procedure
- 6 months following the index procedure
- 12 months following the index procedure
- Annually thereafter, until 5 years post index procedure

Given the DDs with SAE potential that have occurred within the Endurant Evo trials, the Data Monitoring Committee (DMC) has made additional imaging surveillance recommendations, beyond the required follow-up in the protocol. The additional imaging surveillance recommendations are provided, under separate cover, in the most recent DMC Surveillance and Management letter that has been provided to each investigational site.

In addition to the 40 subjects enrolled to support regulatory approval, approximately 30 additional subjects may be enrolled to support geography-specific regulatory requirements. For these subjects, all inclusion/exclusion criteria, study methods, follow-up schedule and data-collected will be identical to the first 40 subjects enrolled.

Number of devices being used within this trial
For subjects that are treated with the bifurcated stent graft minimal 3 pieces will be implanted in the target segment; one bifurcated stent graft component and 2 limb stent graft components. For subjects that are treated with the AUI component approximately 2 pieces will be implanted in the target segment; the AUI stent graft component and one limb stent component. Additional stent graft extensions might be needed to cover the complete target lesion length.

C.6 Randomization and blinding

The study is a single arm study, therefore neither randomization nor blinding are applicable to this clinical trial.

C.7 Sample size

A sample of 40 subjects will be enrolled consecutively and analyzed to support regulatory approval. The sample size of 40 subjects is considered adequate to assess the primary safety endpoint, which is defined as the proportion of subjects experiencing a MAE within 30 days post-implantation. Considering the reported MAE rate from the ENGAGE Post-Approval Study (PAS), which evaluated the long-term safety and effectiveness of the Endurant Stent graft system in 328 subjects[18], it is estimated that 2 of 40 (5%) subjects treated with Endurant Evo AAA stent graft system will experience a MAE. The precision of this assumed 5% point estimate can be assessed by calculating the difference from the 1-sided 95% upper confidence limit. This difference, or margin of error, is calculated to be < 10% for the Endurant Evo International Clinical Trial and is therefore considered adequate to assess the primary safety endpoint.

C.8 Number of investigational sites and study duration

Approximately 10 sites will participate in the clinical study. For the initial 40 subjects to be analyzed, no more than 20% (i.e. 8 subjects) will be enrolled from a single investigational site. Enrollment will be halted at sites that reach the 20% enrollment cap. Following enrollment of the 40 subjects, a site where enrollment has been halted may resume enrolling until approximately 30 additional subjects have been reached in total. For the total cohort (approximately 70 subjects) again no more than 20% of the subjects will be enrolled from a single investigational site.[1]

The total enrollment period is not expected to exceed 12 months. All enrolled subjects will be followed until 5 years post-implantation. Thus total study duration from first subject enrolled to final subject exit could approach 6 years.

A list of names and addresses of the investigational sites and principal investigators in which the clinical study will be conducted will be kept separate from the clinical investigation plan and provided to the investigators. The sponsor will maintain an updated list.

D SUBJECT SELECTION

D.1 Inclusion criteria

Candidates for the Endurant Evo International Clinical trial must be appropriate subjects for endovascular repair of infrarenal abdominal aortic aneurysms or aortoiliac aneurysms (evidenced by screening contrast-enhanced CT or MRA) and have to fulfill all of the following inclusion criteria to be eligible for enrollment in the study:

1) Subject is ≥18 years old
2) Subject understands and voluntarily has signed and dated the Informed Consent approved by the Sponsor and by the Ethics Committee/Institutional Review Board
3) Subject is able and willing to comply with the protocol and to adhere to the follow-up requirements
4) Subject is a suitable candidate for elective surgical repair of AAA as evaluated by American Society of Anesthesiologists (ASA) Physical Status Classification System I, II, or III
5) Subject has an infrarenal abdominal aortic or aortoiliac aneurysm characterized by one or more of the following:
    a) Aneurysm is >5 cm in diameter (diameter measured is perpendicular to the line of flow)
    b) Aneurysm is 4 – 5 cm in diameter and has increased in size ≥0.5 cm within the previous 6 months
6) Subject meets all the following anatomical criteria as demonstrated on contrast-enhanced CT or MRA imaging:
    a) Proximal neck length of ≥ 10 mm with ≤ 60° infrarenal and ≤ 45° suprarenal neck angulation or Proximal neck length of ≥ 15 mm with ≤ 75° infrarenal and ≤ 60° suprarenal neck angulation
    b) Subject has vascular dimensions, e.g., aortic and iliac diameters, lengths from renal arteries to iliac bifurcation and hypogastric arteries, in the range of sizes available for the Endurant Evo AAA stent graft system (measured intima to intima) and within the sizing recommendations (refer to Endurant Evo AAA stent graft system Instructions for Use (IFU))
    c) Subject has a proximal aortic neck diameter ≥ 18 mm and ≤ 32 mm
    d) The distal fixation center of the iliac arteries must have a diameter ≥ 7 mm and ≤ 25 mm bilaterally for the bifur and unilaterally for the AUI
    e) Subject has documented imaging evidence of at least one patent iliac and one femoral artery, or can tolerate a vascular conduit that allows introduction of the Endurant Evo AAA stent graft system
    f) Subject has distal non-aneurysmal iliac (cylindrical) fixation length ≥20 mm bilateral for the bifur and unilaterally for the AUI

[1] Given the DDs with SAE potential that have occurred within the Endurant Evo trials (transition stent fracture, partial suprarenal stent detachment, and suprarenal stent fracture), enrollment was terminated with a total enrollment of 69 subjects.

D.2 Exclusion criteria

Candidates who meet any of the following exclusion criteria will not be eligible for enrollment in the study:

1) Subject has a life expectancy ≤1 year
2) Subject is participating in another investigational drug or device study which would interfere with the endpoints and follow-ups of this study
3) Subject is pregnant
4) Subject has an aneurysm that is:
    a) Suprarenal/pararenal/juxtarenal
    b) Isolated ilio-femoral
    c) Mycotic
    d) Inflammatory
    e) Pseudoaneurysm
    f) Dissecting
    g) Ruptured
    h) Leaking but not ruptured
5) Subject requires emergent aneurysm treatment
6) Subject has a known, untreated thoracic aneurysm >4.5 cm in diameter at the time of screening

7) Subject has been previously treated for an abdominal aortic aneurysm
8) Subject has a history of bleeding diathesis or coagulopathy
9) Subject has had or plans to have an unrelated major surgical or interventional procedure within 1 month before or after implantation of the Endurant Evo AAA stent graft
10) Subject has had a myocardial infarction (MI) or cerebral vascular accident (CVA) within 3 months prior to implantation of the Endurant Evo AAA stent graft
11) Subject has a conical neck defined as a >4 mm distal increase from the lowest renal artery over a 10 mm length
12) Subject has a known allergy or intolerance to the device materials
13) Subject has a known hypersensitivity or contraindication to anticoagulants, antiplatelets, or contrast media, which is not amenable to pre-treatment
14) Subject has significant aortic thrombus and/or calcification at either the proximal or distal attachment centers that would compromise fixation and seal of the device at the discretion of the investigator
15) Subject has ectatic iliac arteries requiring bilateral exclusion of hypogastric blood flow
16) Subject whose arterial access site is not anticipated to accommodate the diameter of the Endurant Evo AAA stent graft delivery system (13F-17F) due to vessel size, calcification, or tortuosity
17) Subject is morbidly obese or has other documented clinical conditions that severely inhibit radiographic visualization of the aorta at the discretion of the investigator
18) Subject has active infection at the time of the index procedure documented by e.g. pain, fever, drainage, positive culture and/or leukocytosis considered to be clinically significant per investigator discretion
19) Subject has congenital degenerative collagen disease, e.g., Marfan's Syndrome
20) Subject has a creatinine level > 2.00 mg/dl (or >176.8 µmol/L)
21) Subject is on dialysis

E STUDY PREPARATION PROCEDURES

E.1 Investigator / Investigational site selection

E.1.1 Investigator selection criteria

The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical study as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical study.
An investigator may be included in the clinical study if compliant with the following requirements:

- Investigators are appropriately qualified practitioners and experienced in the diagnosis and treatment of subjects requiring an endovascular procedure with an abdominal stent graft
- Investigators have adequate time to follow up on the clinical study
- Investigators are willing to comply with the clinical investigation plan
- Investigators are willing to sign the appropriate clinical trial agreement
- Investigators have past experience with conducting clinical studies or appropriate training
- Investigators are familiar with ISO14155:2011 requirements
- Investigators are willing to undergo auditing by sponsor or regulatory bodies
- Investigators are willing to undergo study specific training

E.1.2 Investigational site selection criteria

An investigational site may be selected for participation in the clinical study if compliant with the following requirements:

- Adequate staff (sub-investigator and/or research coordinator) that is accessible and has time to manage the trial and data reporting requirements
- Site personnel has demonstrated experience with conducting clinical (specifically device) trials that comply with applicable regulatory standards
- Site has sufficient annual case volume of AAA stent graft procedures

- Ability to securely store devices according to the Instructions for Use

E.1.3 Clinical Trial Agreement

A clinical trial agreement shall be in place, signed by the participating investigational site and/or principal investigator of each investigational site, as per the local legal requirements, and returned to Medtronic prior to the commencement of any clinical study activities. The investigator is indicating approval of the clinical investigation plan and subsequent amendments, with a fully executed agreement.

E.1.4 Curriculum Vitae

A current (within 3 years) signed and dated Curriculum Vitae from all key members of the investigational site team participating in this clinical study as listed on the Delegated Task List shall be obtained, evidencing the required qualifications, including the year and where obtained, and including their current position at the investigational site.
The signature on the CV must be dated within 3 years prior to the date of activation of the investigational site.

E.2 Ethics

E.2.1 EC/IRB approval

Prior to enrolling subjects in this clinical study, each investigational site's EC/IRB will be required to approve the current Clinical Investigation Plan, Investigator's Brochure, the Informed Consent Form, including any other written information to be provided to the subjects and, if applicable, materials used to recruit subjects. EC/IRB approval of the clinical study must be received in the form of a letter and a copy provided to Medtronic before commencement of the clinical study at an investigational site. The approval letter must contain enough information to identify the version or date of the documents approved. If this information is not contained in the approval letter, it must be retrievable from the corresponding submission letter. In addition the approval letter needs to be accompanied by an EC/IRB roster or letter of compliance, to allow verification that the investigator, other investigation site personnel, and/or Medtronic personnel are not members of the EC/IRB. If they are members of the EC/IRB, written documentation is required stating that he/she did not participate in the approval process. If the EC/IRB imposes any additional requirements (e.g. safety reports, progress reports), the site must request these additional requirements in writing, and then Medtronic will prepare the required documents and send them to the investigator for reporting to the EC/IRB. Investigators must inform Medtronic of any change in status of EC/IRB approval once the investigational site has started enrollment. If any action is taken by an EC/IRB with respect to the investigation, that information will be forwarded to Medtronic by the respective investigator.

E.2.2 Informed consent process

The investigator or authorized designee must obtain written informed consent before any clinical study related activity takes place. In order to ensure the subject has sufficient time to review the materials, prior to the consent discussion, the subject should receive the EC/IRB approved Informed Consent Form. During the consent discussion the investigator or his/her authorized designee must fully inform the subject of all aspects of the clinical study that are relevant to the subject's decision to participate in the clinical study. If a subject is unable to read and/ or write, an impartial witness must be present during the entire informed consent discussion. All items addressed in the Informed Consent Form must be explained. The language used shall be as non-technical as possible and must be understandable to the subject and the impartial witness, where applicable.

The subject must have ample time and opportunity to read and understand the Informed Consent Form, to inquire about details of the clinical study, and to decide whether or not to participate in the clinical study. All questions about the clinical study should be answered to the satisfaction of the subject.

Neither the investigator, nor the investigation site staff shall coerce or unduly influence a subject to participate or to continue to participate in the clinical study. The informed consent process shall not waive or appear to waive the subject's rights.
When the subject decides to participate in the clinical study, the Informed Consent Form must be signed and personally dated by the subject and the investigator or authorized designee. If applicable, the witness shall also sign and personally date the consent form to attest that the

information in the Informed Consent Form was accurately explained and clearly understood by the subject, and that informed consent was freely given.

After all persons have signed and dated the Informed Consent Form the investigator must provide the subject with a copy of the signed and dated Informed Consent Form.

The date when the subject signed the Informed Consent From and the name of the clinical study for which the consent was signed should be documented in the medical records of each consented subject.

E.2.3 Revisions in Informed Consent Form

Medtronic will inform the investigators whenever information becomes available that may be relevant to the subject's confirmed participation in the clinical study. The investigator or his/her authorized designee should inform the subject in a timely manner.

If new information becomes available that can significantly affect the subject's future health and medical care, Medtronic will revise the written Informed Consent Form. The revised information will be sent to the investigator for approval by the EC/IRB. After approval by the EC/IRB, if relevant, all affected subjects shall be asked to confirm their continuing informed consent in writing.

E.2.4 Regulatory submission

In countries where submission to the regulatory authority is required per local law, no subjects will be enrolled in the clinical study until the particular regulatory authority has approved the current clinical investigation plan of the clinical study and other documents as required according to the local requirements.

If the regulatory authority imposes any additional requirements (e.g., safety reports, progress reports) Medtronic will prepare the required documents and send them to the respective authority.

Other documents that are referred to in this clinical investigation plan are listed below and will be made available upon request:

- Monitoring Plan
- Data Management Plan
- Informed Consent Form
- Case Report Forms

E.3 Regulatory compliance

The Endurant Evo International Clinical Trial will be conducted in compliance with the Declaration of Helsinki (October 2013). The international standard ISO 14155:2011 ('Clinical Investigation of medical devices for human subjects') and Medical Device Directive 93/42/EEC will be followed with the following two exceptions:

- ISO 8.2.4.5 Routine on-site monitoring visits will be replaced by remote monitoring (see section (G2 and rationale in L5)
- ISO6.4.1 Adverse events: Not all adverse events will be collected (see section F6 and rationale in L5)

In addition, the study will be compliant with the laws and regulations of the countries in which the clinical study is conducted, including data protection laws, the clinical trial agreement and the clinical investigation plan. In addition, the study will be conducted in compliance with 21 CFR Part 11 and 54 in all participating geographies.

All principles of the Declaration of Helsinki have been implemented in this clinical study by means of the informed consent process, EC/IRB approval, study training, clinical trial registration, preclinical testing, risk benefit assessment and publication policy.

The sponsor will avoid improper influence on, or inducement of the subject, monitor, and investigator(s) or other parties participating in, or contributing to, the clinical study by implementing the informed consent process, clinical trial agreements, and EC/IRB approval.

This study will be publicly registered accordance with the Declaration of Helsinki on www.clinicaltrials.gov.

In case of conflicting requirements, the regulation affording the greatest protection to the subject will be followed.

E. 4 Training requirements

Prior to investigation site activation or subsequent involvement in clinical study activities, the sponsor will provide clinical study training relevant and pertinent to the involvement of personnel conducting clinical study activities. At a minimum, investigator responsibilities, ISO 14155:2011, the clinical investigation plan, Informed Consent Form, use of data collection tool, as well as applicable local regulations are required. Furthermore investigators that will perform the index procedure and implantation of the device will be trained on the Endurant Evo AAA stent graft system. Study- specific training will be documented prior to investigational site activation.

Medtronic and/or its designees are responsible for the training of appropriate clinical site personnel, including the investigator, co-investigator(s), study coordinator(s), and as necessary other site personnel. Initial training will be conducted by Medtronic or its designees at a site initiation visit and/or Investigator meeting to ensure proper reporting of adverse events, uniform data collection and compliance with the protocol, consent processes and applicable regulations.

Also after initial training, Medtronic will provide training to other clinical site study team members. Once the primary endpoint has been reached for all subjects, qualified investigators may also provide training to other clinical site study team members. All study specific training must be documented on a formal training record that will be provided by Medtronic.

E. 5 Clinical study materials

Medtronic will provide study materials to the site after approval of the site for participation. Before a study site can enroll a subject or have access to the electronic data capture (EDC) system, the investigator must be in receipt of an “Activation Letter” (this may be an email, fax or other written communication means) from Medtronic.

E. 6 Study device/product traceability

E.6.1 Supply of investigational devices/products

Once the site has been activated and an eligible subject has been identified and consented through the protocol required screening process investigational devices/products will be ordered and shipped to the site.

E.6.2 Storage and handling of investigational devices/products

Investigational devices/products must be stored in a secured area. The method of storage shall prevent the use of investigational devices/products for other applications than mentioned in this clinical investigation plan. In addition, all information for the use, storage, and handling of the investigational device/product as indicated in the Investigator’s Brochure and Instructions for Use must be taken into account.

E.6.3 Device explant and return procedures/products

All non-functioning or explanted investigational devices/products should be returned to Medtronic for analysis. Information pertaining to the explant procedure should be recorded. If a product is explanted and not returned to Medtronic, an explanation should be provided. The final disposition of the device must be recorded on the device disposition log. Relevant information should also be recorded on associated case report forms, e.g., Adverse Event and Study Exit Form. Detailed instructions for the return of non-functioning devices and explant of the device will be provided in the investigational site file.

E.6.4 Device/product disposition requirements

Investigational devices/products will be traced during the clinical study by assigning unique identifiers to each device/product. The investigator is responsible for maintenance of a Device Tracking Log in the investigator site file. On this log, the receipt, use, return, and disposal of the investigational devices/products shall be documented. At the end of the clinical study the principal investigator must sign and date the original Device Tracking Log.

F STUDY METHODS

F.1 Point of Enrollment

Pre Screening:
Investigators will assess potential subjects with an infrarenal abdominal aortic or aortoiliac aneurysm for their suitability for enrollment in the trial. Initial subject eligibility will be determined by the investigator based upon review of their medical history, disease progress and anatomic suitability for inclusion in the trial as evidenced on screening contrast-enhanced CT/MRA. If the subject appears to meet the eligibility criteria, then the investigator will discuss the study with the potential subject and provide information related to the potential risks and benefits, and required follow-up procedures per the informed consent process.
Test results that are within the timeframes specified below may be used even though the actual test was done prior to a subject's informed consent. This may be done only for standard of care tests with the intent to minimize stress and discomfort to the subject and reduce costs. Required screening evaluations include the following.

- Screening CT or MR with contrast (2 cm above the origin of the celiac artery through the bifurcation of the femoral arteries) (completed within 6 months prior to the index procedure).
- Laboratory tests (completed within 45 days prior to the index procedure) including serum creatinine (required for all subjects) and INR (only required for subjects taking Warfarin preoperatively).

Screening/Baseline Assessments:
After the subject voluntarily has signed and dated the Informed Consent Form, the subject will be considered a study candidate. If a subject does not sign the Informed Consent Form, then no further study specific screening procedures can occur.
Collection of screening and baseline information will take place only after the subject has given voluntary, documented informed consent and will include the following:

- Subject demographics
- Medical history
- Concomitant medication
- Current health status
- Risk factors
- ASA Physical Status Classification
- Laboratory analyses (serum creatinine (required for all subjects), INR (only required for subjects taking Warfarin preoperatively))
- EQ5D Questionnaire

Screening CT/MRA images will be sent to a core lab to assess the anatomical inclusion/exclusion requirements. An Independent Physician Reviewer (IPR) will review screening CT/MRA images to determine eligibility. Approval by the IPR must be obtained prior to a subject's enrollment in the study. The decision of the IPR will be communicated to the investigational site by the Sponsor. Those subjects who sign and date the Informed Consent, meet all study eligibility criteria, and are approved by the IPR will be eligible for enrollment. Subjects that are not approved by the IPR are considered screen failures and will not be enrolled in the study.

Subjects who do not qualify for enrollment will be documented as ineligible on the Screening and Enrollment log.

Enrollment:
Those subjects who sign and date the informed consent document, meet all of the study eligibility criteria, and are approved by the IPR will be eligible for enrollment into the Endurant Evo International Clinical Trial. The subject will be considered to be enrolled when arterial access has been established with an attempt to introduce the Endurant Evo AAA stent graft.
Enrolled subjects will be documented on the Screening and Enrollment Log. Subjects who are enrolled, but not implanted with the device will be followed through the 1 month follow-up only.
The investigator will maintain a log of all subjects screened and enrolled in the clinical study, assigning an identification code linked to their names, alternative subject identification or contact information.

F.2 Implant and Follow up

F.2.1 Index Procedure

All investigators will read, understand and be trained to the Endurant Evo AAA stent graft system Instructions for Use (IFU) prior to initiation of the procedure. The IFU is packaged with the device and must be followed for implantation of the stent graft system.
Identification and/or serial numbers for all investigational components of the Endurant Evo AAA stent graft system used or opened during the index procedure will be recorded.
Adverse event assessment should be done for all subjects as of the moment the subject is considered to be enrolled in the study.

F.2.1.2 Treatment failure
Inability to implant the Endurant Evo AAA stent graft system following arterial access due to deployment issues or entrapment of the delivery system will be considered a treatment failure. These subjects will be followed through the 1-month follow-up time point and then exited from the study.
If a primary conversion to open repair is required during the index procedure, then the subject will be followed for 1 month, at which time the subject will be exited from the study.

After exiting the study, subjects will be followed as per their institutional standard of care.

F.2.2 Hospital Discharge
The following assessments and procedures will be performed and respective data will be collected at hospital discharge:
- Adverse event assessment
- Duration of intensive care unit stay after index procedure (in hours)

F.2.3 Follow-Up Visits and Procedures
Each subject will have required post-implantation follow-up visits at 30-days, 6-month, 12-months, and annually thereafter until 5 years post implantation. Follow-up visits and associated timeframe windows are summarized in Table F-1. Given the DDs with SAE potential that have occurred within the Endurant Evo trials, the Data Monitoring Committee (DMC) has made additional imaging surveillance recommendations, beyond the required follow-up in the protocol. The additional imaging surveillance recommendations are provided, under separate cover, in the most recent DMC Surveillance and Management letter that has been provided to each investigational site.

Table F-1: Post-Implantation Follow-Up Schedule and Windows

Follow-Up Visit	Window Start Day	Target Day	Window Close Day
1 Month (± 15 days)	15	30	45
6 Month (± 30 days)	153	183	213
12 Months (-30/+56 days)	335	365	421
24 Months (±56 days)	675	731	787
36 Months (±56 days)	1040	1096	1152
48 Months (±56 days)	1405	1461	1517
60 Months (±56 days)	1770	1826	1882

At all required follow-up visits subjects will undergo the following assessments:

- Physical Exam (to be reported in FUP eCRF until 24 months only)
- CT/MR with contrast and non-contrast (2 cm above the origin of the celiac artery through the bifurcation of the femoral arteries). At the 6 month follow-up visit: Duplex Ultrasound can be performed if abdominal CT/MR with contrast is not hospital standard of care.
- Abdominal X-ray (4-view, KUB)
- EQ5D questionnaire (until 12 month F/U only)
- Adverse event assessment
- Concomitant Medication (to be reported in FUP eCRF until 24 months only)

If a CT/MR is acquired at discharge (or before Day 15) due to medical necessity, or at the discretion

of the investigator, it may be used to meet the 1-month follow-up visit CT/MR requirement and acquisition of an additional 1-month CT/MR with contrast would not be required.

Abdominal X-rays should be completed via a four-view kidney, ureter, bladder (KUB) X-ray. Posterior/anterior (PA) and lateral images are recommended for visualization of the stent graft. Ensure the entire device is captured on images for assessment.

If conversion to open repair is required during the follow-up period, then the subject will be followed for 30 days after the conversion, at which time the subject will be exited from the study. Please refer to Device Explant and Returned Procedures/Products section, located in E.6.3 of the protocol.

F.3 Data Collection Requirements

Clinical data will be collected preoperatively to establish eligibility, at baseline, during the index procedure, throughout the hospital stay, and postoperatively at the required (and any interim imaging) follow-up visits described in Section F.2. The data collection schedule is summarized in Table F-2. Imaging source data will be sent to the Core Lab for analysis up to the 60-month follow-up visit. Any interim imaging of the stent graft region but not linked to a study visit should be sent to the Core Lab(e.g. imaging performed as standard of care beyond the protocol required time points and/or when performed further to any issue observed at previous imaging Follow-up). This also includes Interim imaging performed, as recommended per the most recent DMC Surveillance and Management letter. All images taken from the stent graft region must be assessed by the site. Any findings that meet the requirements in the flowchart (Appendix L.5) must be reported on the applicable eCRF. Study data will be collected using electronic case report forms (eCRFs) as described in Section G.1. Clinical investigators must electronically review and approve all eCRFs. The monitoring strategy will be defined in the monitoring plan.

Table F-2: Data Collection Schedule

DATA	Screening/ Baseline	Index Procedure	Hospital Discharge	1-Mo. FU (±15 days)	6-Mo. FU (±30 days)	12-Mo. FU (-30/+56 days)	2 Yr. FU (±56 days)	3-5 Yr. FU (±56 days)
Informed consent	✓							
Inclusion / Exclusion criteria	✓							
Physical examination	✓			✓	✓	✓	✓	
Medical history	✓							
Current health status and risk factors	✓							
Laboratory tests at screening:Creatinine, INR[d]	✓							
Device and procedure information		✓						
Implant adjunctive procedures		✓						
Hospital discharge information			✓					
Medications	✓		✓	✓	✓	✓	✓	
Adverse event assessment		✓	✓	✓	✓	✓	✓	✓
EQ5D questionnaire	✓			✓	✓	✓		
IMAGING								
CT/MR (2cm above origin of celiac artery through bifurcation of femoral arteries) [c]	✓			✓[a, b]	✓[a, e]	✓[a]	✓[a]	✓[a]
Abdominal X-Ray (4-view, KUB)				✓	✓	✓	✓	✓

[a] A CT/MR with contrast and non-contrast is required at each follow-up visit. If a subject is unable to tolerate a CT/MR with contrast due to renal insufficiency or physician discretion, a CT/MR without contrast + duplex ultrasound is the preferred alternative imaging modality and should be performed. If the preferred alternative imaging modality is not possible, a duplex ultrasound + 4-view X- ray should be performed to assess the aneurysm and stent graft integrity

[b] If a CT/MR with contrast is acquired at discharge (or before Day15) due to medical necessity or at the discretion of the investigator, it may be used to meet the 1-month follow-up visit CT/MR requirement and acquisition of an additional 1-month CT/MR with contrast would not be required

[c] CT evaluation may include “3-phase technique”, volume studies, 3-D reconstruction, or computer-aided measurements

[d] INR only required for subjects taking Warfarin preoperatively

[e] If abdominal CT/MR with contrast is not hospital standard of care, Duplex Ultrasound can be performed.

[f] Given the DDs with SAE potential that have occurred within the Endurant Evo trials, the Data Monitoring Committee (DMC) has made additional imaging surveillance recommendations, beyond the required follow-up in the protocol. The additional imaging surveillance recommendations are provided, under separate cover, in the most recent DMC Surveillance and Management letter that has been provided to each investigational site.

F.4 Role of the sponsor representatives

Sponsor representatives may provide support as required for the study, including technical support during implantation. The sponsor representative is an experienced expert of device sizing, placement and the technical features of the device and will advise the implanting physician during the implant procedure if needed. The sponsor representative will not be involved actively during the placement and deployment of the Endurant Evo AAA stent graft system.

F.5 Source documents

Investigators are required to maintain source data of each subject's case history, exposure to the device and clinical follow-ups. Source data is all information in original records, certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation.

Examples of these original documents and data records include, but are not limited to: hospital record (paper and electronic, as applicable), subject's screening documentation, recording media such as CD, DVD, CT or other imaging reports, laboratory reports, device accountability records, worksheets and subject files at other departments. Where paper notes and worksheets are retained, these shall be signed and dated by the member of the investigational site team. Where copies of the original source document as well as print outs of original electronic source documents are retained, these shall be signed and dated by a member of the investigational site team with a statement that it is a true reproduction of the original source document.

The investigator will clearly mark clinical records to indicate that the subject is enrolled in this clinical investigation.

Source documents will be used for verification of the data documented in subject's eCRF during monitoring visits, audits and inspections, and for the adjudication of AEs and must be accessible to the Medtronic field clinical support and the clinical study team.

The investigator will allow inspections of the study site and documentation by Clinical Research and audit personnel from Medtronic or designee, EC/IRB, external auditors, or representatives of regulatory authorities. The purpose of these inspections is to verify and corroborate the data collected on the eCRFs. In order to do this, direct access to medical or clinical records is necessary.

F.6 Adverse Events

For the purpose of this clinical investigation Medtronic will define and classify the following events per ISO14155:2011 (followed for definitions of Adverse Events only)

Adverse event reporting for the remaining follow up (3-5 years) will focus on the reporting of the below listed events:

- Adverse events with a possible, probable or causal relationship to the aneurysm (Excluding aneurysms in anatomic areas other than the Endurant grafted segment)
- Adverse events with a possible, probable or causal relationship to the device
- Adverse events with a possible, probable or causal relationship to the index procedure
- Adverse events leading to subject's death

Secondary procedures performed as a result of any of the above adverse events must be reported on the respective Adverse Event form. Please see guidance for reporting of adverse events following image review in Appendix L.5.

All adverse events that meet the study definitions will be reported to the sponsor and documented on the Adverse Event eCRF and in the subject's medical records.

Clinical events that are inherent to a surgical procedure and expected to occur in the majority of subjects for a projected duration may be considered unavoidable. Such events include, but are not limited to, those listed in Table F-3. These events should not be reported as adverse events during this study.

Table F-3: Expected and un-reportable adverse events related to a surgical procedure

Description of the Event	Time Frame from the Index Procedure
Endoleaks observed and resolved during the index procedure	Resolved by the time the subject leaves the OR
Anesthesia-related nausea and/or vomiting	Within 24 hours
Low-grade fever (< 100° F or < 37.8° C)	Within 48 hours
Back pain related to laying on OR table	Within 72 hours
Incisional pain (pain at access site)	Within 72 hours
Sleep problems, insomnia or post procedural delirium	Within 72 hours
Mild to moderate or bruising or ecchymosis	Within 168 hours

F.6.1 Definitions / Classifications

Adverse Event (AE): *(ISO14155:2011 3.2)*
Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.
NOTE 1: This definition includes events related to the investigational medical device.
NOTE 2: This definition includes events related to the procedures involved.
NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse Device Effect (ADE): *(ISO14155:2011 3.1)*
Adverse event related to the use of an investigational medical device.
NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Serious Adverse Event (SAE): *(ISO 14155:2011 3.37)*
Adverse event that
a) led to death,
b) led to serious deterioration in the health of the subject, that either resulted in
   1) a life-threatening illness or injury, or
   2) a permanent impairment of a body structure or a body function, or
   3) in-patient or prolonged hospitalization, or
   4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
c) led to fetal distress, fetal death or a congenital abnormality or birth defect.

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE): *(ISO 14155:2011 3.36)*
Adverse device effect that has resulted in any of the consequences characteristic of a Serious Adverse Event.

Unanticipated Serious Adverse Device Effect (USADE): *(ISO 14155:2011 3.42)*
Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.
NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

Device deficiency: *(ISO 14155:2011 3.15)*
Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.
NOTE: Device deficiencies include malfunctions, use errors, and inadequate labelling.

F.6.2 Recording and reporting of Adverse Events

Adverse Event (AE) information will be collected throughout the study and reported to Medtronic on the Adverse Event eCRF. The investigator is responsible for reporting all AEs as reportable/collectable per CIP to Medtronic. See the Adverse Event eCRF for the information to be reported for each Adverse Event. Please see guidance for reporting of Adverse Events following image review in Appendix L.5.

For Adverse Events that require immediate reporting (see Table F-4), initial reporting may be done by phone, e-mail (contact details will be provided in the investigational site file), or on the eCRF with as much information as is available. In case the investigator requires information from the Sponsor in an emergency situation, the contact details for emergency situations are given in the investigational site file.

F.6.3 Recording and reporting of Device Deficiencies

Device Deficiency information will be collected throughout the study and reported to Medtronic. Device Deficiencies should be reported on a Device Deficiency Form in the eCRF. In case the eCRF is not available the Device Deficiency form needs to be completed manually and must be sent to Medtronic. Contact details are given in the investigational site file. The investigator is responsible for reporting all Device Deficiencies to Medtronic.

See the Device Deficiency eCRF for the information to be reported for each Device Deficiency.

Device deficiencies that did not lead to an Adverse Event but could have led to an SAE

a) if either suitable action had not been taken,
b) if intervention had not been made, or
c) if circumstances had been less fortunate,

require immediate reporting (see Table F-4). Initial reporting may be done by eCRF, phone, e-mail, with as much information as available*. Please see guidance for reporting of Device Deficiency following image review in Appendix L.5.*

F.6.4 Adverse Event and Device Deficiency review process

All Adverse Events and Device Deficiencies will be reviewed by Medtronic Study Management and/ or designee. This review will include the determination whether the Adverse Event/Device Deficiency meets regulatory reporting requirements. The sponsor will ensure timely Adverse Event/Device Deficiency reporting to meet global regulatory requirements.

In case the Adverse Event/Device Deficiency is related to a Medtronic market released device used during the study, Medtronic Study Management and/ or designee will immediately report this device related Adverse Event/Device Deficiency to the Product Experience Management (PXM) group. The PXM group will ensure prompt review, and appropriate reporting.

Table F-4: Adverse Event Reporting Requirements from Investigator to Medtronic

Serious Adverse Device Effects (SADE), including Unanticipated Serious Adverse Device Effect (USADE):	Immediately (but no later than 3 calendar days) after the investigator first learns of the event or of new information in relation with an already reported event.
Serious Adverse Events (SAE)	Immediately (but no later than 3 calendar days) after the investigator first learns of the event or of new information in relation with an already reported event.
Adverse Device Effects (ADE)	Immediately (but no later than 3 calendar days) after the investigator first learns of the event.
All other AEs	Submit in a timely manner after the investigator first learns of the event.
Device Deficiency (with SAE potential)	Immediately (but no later than 3 calendar days) after the investigator first learns of the deficiency or of new information in relation with an already reported deficiency.
All other Device Deficiencies	Submit in a timely manner after the investigator first learns of the deficiency.

In addition, Investigators are obligated to report adverse events in accordance with the requirements of their IRB/EC and local regulations. The Sponsor is obligated to report adverse events and device deficiencies that occur during this trial to the Regulatory Authorities and IRB/EC as per local requirements. The applicable timeframes are described in the Endurant Evo Clinical Trial safetyplan.

F.6.5 Clinical Event Committee

A clinical event committee (CEC) will be established. The CEC is an independent committee made up of clinicians (interventional and non-interventional) with pertinent expertise who are not participants in the study and who do not have any other real or potential conflicts of interest. The CEC will meet periodically to review and adjudicate all major adverse events (except procedural blood loss), serious unanticipated adverse device effects, and all deaths that occur throughout the conduct of the clinical trial. A charter will be developed that will detail the criteria for selected

complications and clinical events that need to be adjudicated as well as the CEC composition, duties, procedures and adjudication rules and meeting frequency.

F.6.6 Emergency contact details in case of serious AEs

In case of an immediately reportable Adverse Event the investigators can contact the Medtronic Study Manager. Contact details of Medtronic Study Management are given in the Investigational Site File. In case the investigator requires information in a medical emergency situation the investigator can contact the Medical Expert. Contact details of Medical Expert are given in the Investigational Site File.

F.7 Subject accountability

Every subject should be encouraged to remain in the study until they have completed the required follow up per the study protocol. If the subject discontinues prematurely from the study (e.g. withdrawal of the consent, lost to follow-up), the reason for discontinuation must be documented in the subject's hospital record and documented on the appropriate eCRF. Subjects will not be replaced in case of premature study discontinuation.

F.7.1 Criteria and procedures for exit from study

The Study Exit eCRF should be completed after the subject is exited from the study. A subject will be considered to have exited from the study for any of the following reasons:

- Subject completes follow-ups required by the investigational plan
- Subject dies
- Subject requests to be withdrawn
- Investigator requests that subject be withdrawn to protect the welfare of the subject
- Subject is lost to follow-up
- Subject has conversion to open repair
- Other (specify).

F.7.2 Study Withdrawal

Subjects may withdraw from the clinical study at any time and for any reason. If a subject decides to withdraw from the clinical study and agrees to provide the reason for withdrawal, the investigator will document the reason and indicate any relationship of the withdrawal to the study or products being investigated in the subject's hospital record in the subject's file. If discontinuation is because of safety or lack of effectiveness, the subject shall be asked to be followed as per their institution's standard of care outside the clinical study as further described in section F.7.6. In addition, subject withdrawal will be documented on the Study Exit eCRF.

F.7.3 Missed follow-up

A missed follow-up visit should be documented by the investigator and reported in the eCRF including the reason. If the date the subject is last known to be alive is obtained, this should be recorded on the Follow-up visit eCRF and the method of obtaining this date should be documented in the medical record.

F.7.4 Lost-to-follow-up

A subject may be considered lost to follow-up once the investigator and/or research staff has made three documented attempts to contact the subject. The third attempt should be made by certified mail to the subject.

F.7.5 Conversion to open repair

If a primary conversion to open repair is required during the index procedure, then the subject will be followed for 1 month, at which time the subject will be exited from the study.

If a secondary conversion to open repair is required during the follow-up period, then the subject will be followed for 30 days after the conversion, at which time the subject will be exited from the study.

F.7.6 Medical care after study exit

After study exit the subjects will be followed as per routine standard of care by the investigational site or a treating physician which might be in line with the guidelines described in the *Management of Abdominal Aortic Aneurysms Clinical Practice Guidelines of the European Society for Vascular Surgery*[19] or *Society for Vascular Surgery practice guidelines for the care of patients with an abdominal aortic aneurysm*[20].

Relevant medical records may be made available by the investigational sites for the treating physician per local laws and regulations if needed for further subject treatment. As per local law and regulation the trial investigator may be contacted by the treating physician in case of questions related to the study device and treatment.

F.8 Study/Protocol deviations and CIP changes

A study deviation is an event where the investigator or investigation site personnel did not conduct the clinical study according to the clinical investigation plan or clinical trial agreement. The investigator is not allowed to deviate from the above mentioned documents except with prior approval and/ or under emergency circumstances. All deviations shall be documented and explained, regardless of the reason for the deviation.

Specific examples of deviations include but are not limited to:

- Failure to obtain informed consent prior to participation
- Incorrect version of the informed consent form used
- No EC approval before the start of the study
- Enrolled subject did not meet inclusion/exclusion criteria
- CIP required testing and/or measurements not done or incorrectly done subject did not attend follow up visit or follow up visit outside window
- Unauthorized use of investigational devices
- Adverse event not reported by investigators in the required time frame as specified in the CIP
- Control of study devices not maintained
- Source data lost or unavailable
- Enrollment of subjects during elapse of IRB/EC approval
- Subject not implanted according to the Instructions for Use

Medtronic will assess the significance of all deviations and evaluate the need to amend the clinical investigation plan or to early terminate the investigation, in accordance with Medtronic SOPs.

F.8.1 Request for approval of study deviations

The investigator shall obtain documented approval from Medtronic before implementation, for any change or deviation from the clinical investigation plan. In case of study deviations that can affect the subject's rights, safety or well-being or the scientific integrity of the clinical study, approval from the EC/IRB and regulatory authority must also be obtained before implementation. The investigator shall timely contact the Clinical Study Manager for review of the proposed change/deviation.

Prior approval is not always realistic in situations where unforeseen circumstances are beyond the investigator's control. However, also in these cases, the event is considered a deviation, and shall

be reported.
In any emergency situation the investigator shall exercise his/her judgment to safeguard the subject's interest. Such deviations from the clinical investigation plan do not require the prior approval of Medtronic. The investigator shall report the deviation as soon as possible to Medtronic and the reviewing EC/IRB, if applicable. Medtronic will inform the regulatory authorities, if required.

F.8.2 Reporting requirements for study deviations

Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the CIP, additional training, terminate the study), such as those included in, but not limited to, the list below. Repetitive or serious investigator compliance issues may result in the need to initiate a corrective action plan, and in some cases freeze enrollment or ultimately terminate the investigator's participation in the clinical study:

- Non-compliance to obtain subject's informed consent
- Non-compliance to the inclusion/exclusion criteria
- Failure to follow subjects per scheduled follow-ups
- Failure to follow-up with findings on monitoring reports
- IRB/ EC approval expiration
- IRB/ EC suspension of the center

If a center is terminated or suspended, no additional enrollments will be allowed at the center. Unused investigational product allocated to the center will be returned to Medtronic.
Medtronic will provide site-specific reports to the investigators on a periodic basis summarizing information on deviations that occurred at the investigational site.
The investigator shall adhere to EC/IRB requirements and procedures for reporting study deviations.

F.8.3 Amendments to the Clinical Investigation Plan

The investigator can propose any appropriate modification(s) of the clinical investigation plan or investigational device or investigational device use. Medtronic will review this proposal and decide whether the modification(s) will be implemented.
Medtronic will submit any significant amendment to the clinical investigation plan, including a justification for this amendment, to the appropriate regulatory authorities and to the investigators to obtain approval from their EC/IRB. The investigator will only implement the amendment after approval of the EC/IRB, regulatory authority and Sponsor. Administrative amendments to the clinical investigation plan will be submitted to the EC/IRB for notification. Furthermore investigators shall sign any approved amendment of the clinical investigation plan, if required per local regulation.

G QUALITY CONTROL PROCEDURES

G.1 Procedures for database management

G.1.1 Data collection

The investigator must ensure accuracy, completeness and timeliness of the data reported in the eCRFs and in all other required reports. Data reported on the eCRFs which are derived from source documents must be consistent with the source documents and discrepancies need to be justified in a documented rationale, signed and dated by the principal investigator or co-investigator, and filed in the subject's medical file.
Only authorized persons can complete eCRFs. The investigator (physicians only) shall sign eCRFs as specified on the Delegated Tasks List/ Delegation of Authority Form included in the Investigator Site File.
The Electronic Data Capture (EDC) system maintains an audit trail on entries, changes, or corrections in eCRFs. If a person is only authorized to complete eCRFs or to make changes to an already signed eCRF, the investigator shall re-sign this eCRF.
Any source documentation as well as any imaging (e.g., procedure reports, imaging material, lab reports, death certificates, autopsy reports) that is sent to the sponsor should have all subject

identifiers removed and replaced with the subject's study ID.
A paper copy of the eCRFs as well as access to the EDC system will be provided to the investigation site prior to subject enrollment.

G.1.2 Source data to be directly recorded on the Case Report Forms

All data reported on the eCRFs shall be derived from source documents and be consistent with these source, and any discrepancies shall be explained in writing. There are no data that will be recorded directly on the eCRF without corroborating source documentation.

G.1.3 Time windows for completion and submission of Case Report Forms

All data entry should be completed as soon as possible after the visit takes place. Adverse event and device deficiencies should be reported as described in the section F.6.

G.1.4 Data review and processing

Data management will be done according to Medtronic SOPs and the Data Management Plan for this clinical study. These documents will be made available on request.
All collected data will be reviewed for completeness, correctness and consistency. In case of issues, queries will be sent to the investigator or designee to complete, correct or comment the data.

G.2 Monitoring procedures

A site qualification visit may be conducted by Medtronic personnel (or designees) to review the clinical investigational plan and, regulatory and study requirements with the investigator and study personnel. A site initiation visit will be performed after it has been verified that the site is prepared for the study and that the site requirements for study participation are met.
On-site Monitoring visits will be conducted at the start and during the clinical study in accordance with Medtronic SOPs and the Monitoring Plan. Frequency and timing of monitoring visits shall be determined by the Sponsor for each site based on enrollment rate and volume, study compliance and findings from previous visits.
In-person monitoring visits will be replaced by telephone and email contact to the sites by the study team. The sponsor monitoring phone calls will include an assessment of the source documents to assure completeness of image submissions and event reporting and an assessment of the essential documents. In particular, the focus of these calls will be to ensure that safety data is entered and to verify that all relevant events are reported. Site monitoring visits will be requested by the Sponsor if a concern arises with regards to compliance or data integrity

It will be verified whether signed and dated informed consent forms have been obtained from each subject before any clinical study related procedures are undertaken. Medtronic or designee will conduct site monitoring visits to monitor compliance with the protocol and adherence to the data collection procedures, to assess the accuracy and completeness of submitted clinical data, and to verify that records and documents are being properly maintained for the duration of the study.

G.2.1 Accessibility of investigation site staff and study materials

The principal investigator(s), his/her delegate(s), and the study coordinator(s) shall be accessible to Medtronic personnel or designee(s) and the Clinical Study Manager. This accessibility is of particular importance for reviewing data in the eCRF. Direct access to subject medical files for source data verification will need to be granted and prepared prior to any monitoring visits. If direct access cannot be provided per local laws and regulations, certified copies need to be made available or monitor needs to obtain access by reviewing alongside with study staff.

G.2.2 Audits and investigation site inspections

In addition to regular monitoring visits, Medtronic may conduct audits at participating investigational sites. The purpose of an audit is to verify the adequate performance of the clinical study related activities, independent of the employees involved in the clinical study. Regulatory bodies may also perform inspections at participating investigational sites. Any regulatory authority inspection announcements shall be forwarded immediately to the Clinical Study Manager.

The investigator and/or institution shall permit Medtronic and regulatory bodies direct access to

source data and documents, taking into account any restrictions due to local law, to perform clinical study-related monitoring, audits, EC/IRB review, and regulatory inspections.

G.3 Study suspension or early termination

G.3.1 Early study suspension or termination

Medtronic or regulatory authority may decide to suspend or early terminate the clinical study (e.g. if information becomes available that the risk to study subject is higher than initially indicated, if interim analysis indicates that the results significantly differ from the study objectives or statistical endpoints). If the clinical study is terminated early or suspended, Medtronic shall promptly inform the investigators of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC/IRB and the study subjects.

G.3.2 Early investigation site suspension or termination

Medtronic, EC/IRB, or regulatory authority may decide to suspend or prematurely terminate an investigation site (e.g. in case of expiring approval of the reviewing EC/IRB, non-compliance to the Clinical Investigation Plan or lack of enrollment).

If an investigation site is suspended or prematurely terminated:

- Medtronic shall promptly inform the clinical investigator(s) of the termination or suspension and the reason(s) for this
- The investigator shall then promptly inform the reviewing EC/IRB
- The investigator shall then promptly inform study subjects
- The investigator agreement will be terminated
- The investigator will inform the institution (where required by applicable regulatory requirements)
- Medtronic will inform the regulatory authority(ies) (where required by applicable regulatory requirements)

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definite outcomes, investigators must assess whether to continue, modify or immediately stop the clinical study in the respective investigation site and immediately inform the sponsor and EC/IRB, if applicable.

G.3.3 Subject follow-up in case of termination

If the study is terminated early, subjects will be followed as per routine standard of care by the investigational site or a treating physician which might be in line with the guidelines described in the *Management of Abdominal Aortic Aneurysms Clinical Practice Guidelines of the European Society for Vascular Surgery*[19] or *Society for Vascular Surgery practice guidelines for the care of patients with an abdominal aortic aneurysm*[20].

After study termination relevant medical records may be made available by the investigational sites for the treating physician per local laws and regulations if needed for further subject treatment. As per local law and regulation the trial investigator may be contacted by the treating physician in case of questions related to the study device and treatment.

G.4 Study close out

Prior to completion of study close out, all data must be entered and approved in the EDC system. Medtronic and/or its designees will notify the site of the intention to close the study. Remote study close out visits may be performed. The intent of these visits will be to assure the investigator's regulatory files are up to date and complete and that any outstanding issues from previous visits have been resolved. Medtronic will notify and inform the site(s) that all requirements have been met with a study closure letter.
If required, EC/IRB and/or regulatory authority will be informed by Medtronic about the study close out.

H DATA ANALYSIS AND REPORTING

Any deviations from this section will be described and justified in the final clinical study report, as appropriate.

H.1 Analysis of clinical data

All endpoints will be analyzed descriptively. In general, qualitative parameters will be described by their distribution frequencies; quantitative parameters will be described by their mean, standard deviation, minimum, maximum, median, and number of subjects with assessable data.

The survival from all-cause mortality over one year time or longer will be described by the Kaplan-Meier survival curve and the associated Kaplan-Meier estimate will be calculated along with its standard error using the Greenwood method.

For events such as AEs, deaths and secondary procedures, that can occur or are observed at any time during the study, no time window will be applied. For such events, an event that occurs "within 1 month or 30 days" is an event that takes place between Days 0 to 30, inclusive. Similarly, an event that occurs "within 12 months or 365 days" is an event occurring between Day 0 to Day 365, inclusive. Date of event onset will be used to determine when the event occurred. Day 0 is referring to the day of index procedure.

For image-based assessments, such as stent-graft endoleak, patency, and other observations, the following time windows will be applied for by-visit data summaries:

Table H-1: Time Windows for Statistical Analyses

Study Visit	Target Day	Time Window
Implant	Day 0	Day 0
1 Month	Day 30	1 – 90 days
6 Months	Day 183	91 – 304 days
12 Months	Day 365	305 – 548 days
2 Year	Day 731	549 – 913 days
3 Year	Day 1096	914 – 1278 days
4 Year	Day 1461	1279 – 1644 days
5 Year	Day 1826	1645 – 2009 days

If there are two or more assessments in the same time window, then the assessment closest to the target day will be used in the analysis of event rate at a given time point.

In addition to endpoints, summaries of subject disposition, demographics, baseline characteristics, and subject accountability will be provided.

During statistical analysis, imputation of missing data will not be performed except for data related to the onset date of an adverse event or a death. In cases where the onset date of an event or a death is incomplete and unresolvable via data query, the 15th day of the known month or July 1st of the known year will be used.

Statistical analyses for this study will be performed using the Statistical Analysis System (SAS) for Windows (Version 9.1 or higher) or other widely-accepted statistical or graphical software.
Analysis for the regulatory submission:

For the primary endpoint, a one-sided 95% confidence interval based on binomial distribution will be constructed in addition to event count and frequency. Subset analysis will be performed by-sex for the primary endpoints descriptively and reviewed for clinical significant difference. All analysis will be performed on the intent-to-treat analysis set, which includes all enrolled subjects. Subjects will be considered as enrolled in the study as described in section F.1.

The analysis for the regulatory submission will take place when 40 subjects have been implanted with the study device for at least 30 days except that a subject expires early.[2] Endpoints as defined in Section C.2 will be analyzed for these 40 enrolled subjects.

Interim Analysis:
No interim analysis is planned prior to the regulatory submission.

Annual Report:
An annual report will be provided including all enrolled subjects at the time of reporting if required per local law and regulations.

H.2 Publication Policy

Publications and presentations referring to this clinical study will be coordinated by Medtronic to allow the use of all available data. The following publication policy will have to be adhered to by all participating investigational sites:
Medtronic may use the study data for regulatory authority submission results, may publish the results in peer reviewed scientific journal(s) and present the data at major congresses.
Authorship on any publication(s) resulting from this clinical study will be assigned according to substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published. This is in accordance with the Vancouver principles (The Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, ICMJE, October 2008), as agreed upon by the editors of all major medical journals.
The number of authors will be dependent on the regulations of the concerning journal with a maximum of 10 authors. Names of all participating investigators will appear in the Acknowledgment of the paper.
Based on the principle that Medtronic owns the data of this clinical study, a single investigational site may access and use the data provided by itself for scientific publications following prior approval by Medtronic.
Pooling data from several investigational sites for publication purposes, national projects and international projects all require prior approval from Medtronic.
Medtronic as the owner of the data can use the data and/or any results derived from the data or publications based on that data for marketing purposes, further research and development of devices or educational use.
The study sponsor will collect data in such way that no subject can be identified. Participating subjects will not be identified by name in any published reports about the clinical study.

I STUDY MANAGEMENT

I.1 Study Contact

The study is sponsored by the Medtronic Bakken Research Center B.V. based in the Netherlands. Study staff contact details will be provided in the investigational site file.

I.2 Advisory committees

I.2.1 Clinical Event Committee (CEC)

A clinical event committee (CEC) will be established. The CEC is an independent committee made up of clinicians (interventional and non-interventional) with pertinent expertise who are not participants in the study and who do not have any other real or potential conflicts of interest. Please refer to section F.6.5 for further details regarding the CEC.

[2] Given the DDs with SAE potential that have occurred within the Endurant Evo trials (transition stent fracture, partial suprarenal stent detachment, and suprarenal stent fracture), enrollment was terminated with a total enrollment of 69 subjects.

I.2.2 Data Monitoring Committee

A Data Monitoring Committee (DMC) will be established. The DMC is composed of several members with pertinent expertise who are not participants or directly involved in the conduct of the study.
The responsibility of the DMC is to evaluate safety data during the course of the study and to advise Medtronic about the continuing safety of the study, in order to ensure the well-being of the current participants and those yet to be enrolled as well as the continuing validity and scientific merit of the study. The DMC will review the study data after all subjects have reached the 1-month follow-up time point but might also be reviewed earlier. Thereafter, the study data will be reviewed on a periodic basis as defined in the DMC Charter.

Based on the safety data, the DMC may recommend that Medtronic modify or stop the study. DMC composition, duties, procedures, deliberation rules, are detailed and documented in the DMC Charter.

I.2.3 Publication Committee

A publication committee will not be established for the Endurant Evo Clinical trial. The publication policy for this trial is described in section H.2.

I.2.4 Imaging Core Lab

An imaging core lab will be established to independently analyze images based on the imaging protocol/core lab guidelines. Imaging guidelines will be provided in the investigational site file.

I. 3 Records and reports

I.3.1 Investigator records

At a minimum, the following records must be kept by the investigator:

- Clinical Investigation Plan and, if applicable, any amendments
- Investigator's Brochure and 1 copy of the Instructions for Use
- Medtronic and EC/IRB approved Informed Consent Form
- Regulatory authority approval or notification
- Fully signed Clinical Trial Agreement and confidentiality agreement (if not included in the Clinical Trial Agreement)
- Financial disclosures
- Insurance certificates
- Completed Delegated Task List and Curriculum Vitae of all investigational site personnel
- Training documentation of all investigation site personnel
- Relevant communications
- Subject screening log and/or subject identification log
- Signed, dated, and fully executed Informed Consent Forms
- Fully executed eCRFs and corrections (in the EDC)
- Reports of Adverse Events and Device Deficiencies
- Device accountability records
- IRB/EC correspondence

I.3.2 Investigator reporting responsibilities

Table I-1: Investigator reporting responsibilities

Report	Submitted to	Description

Adverse Events	Sponsor, EC/IRB, and local regulatory authority, where applicable	Refer to section F.6 for reporting requirements.
Progress Report	Sponsor and EC/IRB	Provide if required by local law or IRB/EC. (ISO 14155:2011)
Withdrawal of EC/IRB approval	Sponsor	Investigator will inform Medtronic in case EC/IRB approval is withdrawn.
Final Report	EC/IRB	A copy of the Final Clinical Study Report will be provided to the EC/IRB.
Deviations from Investigational Plan		
Emergency Use	Sponsor, EC/IRB, regulatory authority, if applicable	Investigator will report deviation as soon as possible to the sponsor, EC/IRB and regulatory authority if applicable.
Planned deviation	Sponsor, EC/IRB, regulatory authority, if applicable	Prior approval from Medtronic must always be obtained from Medtronic. If the deviation affects scientific soundness of the clinical study or the rights, safety, or welfare of the subject and is not an emergency, prior approval must be obtained from the EC/IRB and regulatory authority.
Other Deviations	Sponsor, EC/IRB, regulatory authority, if applicable	Deviations that are beyond the control of the investigator (such as subject who fails to return to follow-up visit) or deviations that do not affect the scientific soundness of the clinical study or the rights, safety, or welfare of the subject and are not an emergency, should be submitted as they are identified by the investigational site or Medtronic staff.

I.3.3 Sponsor records

At a minimum, the sponsor will keep the following records:

- All essential study documents and correspondence that pertains to the clinical study
- CIP and, if applicable, any amendments
- Investigator Brochure and one copy of the Instructions for Use
- Sample of labeling attached to the investigational device
- Curriculum Vitae of investigators and investigational site personnel
- Delegated Task Lists and training records of investigators and investigational site personnel
- EC/IRB approvals/notifications/communication and regulatory approvals/notifications/ communication
- Signed Clinical Trial Agreements and signed agreements with third parties
- Insurance certificates
- Shipping records for investigational devices and clinical-investigation related documents and materials
- Medtronic and EC/IRB approved Informed Consent Forms
- Site qualification reports, site initiation reports and monitoring visit reports
- Adverse event and Device Deficiency reports
- Financial disclosure information
- Fully executed eCRFs and corrections

I.3.4 Sponsor reporting responsibilities

Table I-2: Sponsor reporting responsibilities

Report	Submit to	Description
Adverse Events	EC/IRB, Investigators, FDA and regulatory authorities, where applicable	Medtronic will report adverse events as required and in compliance with local regulatory requirements, as applicable and as described in the Endurant Evo Safety Plan.
Withdrawal of EC/IRB approval	EC/IRB, Investigators, FDA and regulatory authorities, where applicable	In case of withdrawal of EC/IRB approval Medtronic will suspend the clinical study as described below.
Premature termination or suspension of study	EC/IRB, Investigators, and regulatory authorities, where applicable	Medtronic will provide prompt notification of termination or suspension and reason(s) to investigator and where required to EC/IRB and regulatory authorities.
Progress Reports	EC/IRB, regulatory authority (upon request)	Progress reports will be submitted to the EC/IRB and/or Regulatory Authority only if required.
Final Report	Investigators, and regulatory authorities, where applicable	Medtronic will provide all investigators with a copy of the Final Clinical Study Report of the clinical study. EC/IRBs and regulatory authorities will be informed when required.
Study deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the case report forms and the final report of the clinical investigation.
Emergency Deviations from Investigational Plan	Regulatory authorities, where applicable	If required, Medtronic will inform regulatory authorities as soon as possible about any emergency deviations that affect scientific soundness of the clinical study or the rights, safety, or welfare of the subject.
Significant new information	EC/IRB and regulatory authority	Ensure that the EC/IRB and Regulatory Authorities are informed of significant new information about the clinical investigation (ISO 14155:2011).

I.3.5 Record retention

The investigator must retain the Investigator Site File, subject medical files and CRFs in accordance with local law and regulations for a minimum period of 2 years (or longer if local laws require) after market-release in his/her region and after study closure. The investigator should take measures to prevent accidental or early destruction of the clinical study related materials.

I. 4 Miscellaneous

I.4.1 Insurance

The Medtronic Bakken Research Center B.V. is a wholly owned subsidiary of Medtronic Inc., which as the parent company of such entity maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a Clinical Trial Insurance statement/certificate will be provided to the EC/IRB and the regulatory authorities.

I.4.2 Subject compensation and indemnification

Medtronic shall reimburse the institution/hospital in which the subjects are treated for reasonable

and necessary travel expenses incurred by the subjects enrolled in the study including, but not limited to travel to/from the hospital, provided that such expenses are properly documented in the subject files and that the study evaluation is not performed under a regularly scheduled follow-up. These expenses will be payable to the institution/hospital upon receipt by Medtronic of a detailed invoice, which, however, shall not contain any identifying characteristics concerning the subjects. Finally the site in which the subject is treated shall be solely responsible for the reimbursement of expenses directly to the subject.

I.4.3 Subject confidentiality

Subject confidentiality will be maintained throughout the clinical study to the extent permitted by law. That is, every attempt will be made to remove subject identifiers from clinical study documents. For this purpose, a unique subject identification code (site number and subject number) will be assigned and used to allow identification of all data reported for each subject. This will also ensure that the information can be tracked back to the source data.

Study data may be made available to third parties, e.g., in the case of an audit performed by regulatory authorities, provided the data are treated confidentially and that the subject's privacy is guaranteed. The identity of a subject will never be disclosed in the event that study data are published.

J RISKS AND BENEFITS

J.1 Potential Risks

Appendix L.3 shows a list of potential adverse events that may be associated with use of the Endurant Evo AAA stent graft system. The occurrence of the listed complications may lead to a repeat endovascular intervention and/or open surgical repair. Since the Endurant Evo AAA stent graft system is an investigational device, all risks may not be known. Risk mitigation activities were performed during development and design verification tests of the device. Activities intended to minimize risks during the conduct of the clinical trial include the following:

- Investigator and study personnel will be trained to the design of the Endurant Evo AAA stent graft system, its application, and preclinical results.
- Eligibility criteria and screening procedures will be followed to ensure that appropriate subjects are enrolled.
- Investigator will adhere to the Endurant Evo AAA stent graft system IFU packaged with the device.
- The subjects will be carefully monitored throughout the study period.
- The investigator will evaluate the subject adverse events during the course of the study.
- Data submitted from the investigative centers will be monitored during the course of the study.
- Monitoring visits will be conducted to evaluate protocol compliance and data quality.
- Safety and effectiveness data obtained during the course of the study will be shared with investigators in periodic reports to increase understanding of the device and potential adverse events.
- A Data Monitoring Committee, Clinical Events Committee, and imaging core lab will be established to independently evaluate subject health status, device performance, and identify any safety concerns regarding subjects' well-being.

If a woman is pregnant or becomes pregnant, implantation of the trial device may involve risks to the embryo or fetus that are unknown at this time. Therefore, pregnant women will be excluded from the study. If a female subject becomes pregnant during the conduct of this clinical research study they need to inform the investigational site immediately. The risks will be continuously monitored, assessed and documented by the investigator. Any unanticipated or unforeseen complications will be reported by the investigator (or authorized designee) to the IRB/ EC and to Medtronic. Medtronic will in turn report any necessary findings to the appropriate regulatory agencies in each of the respective geographies.

J.2 Potential Benefits

The potential benefits of the Endurant Evo AAA stent graft system have not been documented; nevertheless, they are expected to be similar to those associated with endovascular stent graft systems currently in clinical trials or commercially available. Endovascular treatment of AAA has been shown to be an effective, less invasive procedure that may result in a reduced rate of early mortality and comorbidities associated with open surgical repair[12,21,22]. Stent graft repair also provides a treatment option for subjects who would not otherwise be eligible for surgical repair.
Additional potential benefits include the following:

- Reduced operating room and anesthesia time
- Reduced requirement for blood transfusions
- Shorter time in intensive care
- Shorter length of hospital stay
- Shorter recovery time and return to activities of daily living
- Reduced access complications
- Ability to treat subjects with smaller iliac anatomy
- Ability to use percutaneous access for treatment

J.3 Risk-to-Benefit Rationale

The benefits and risks associated with Medtronic's AAA stent grafts are well-characterized through robust history of testing and successful clinical results. The Endurant Evo AAA stent graft system is Medtronic's fourth generation AAA stent graft which is not only designed using established design characteristics and long term experience from previous generation Medtronic stent grafts but also uses the same principles of operation and technological characteristics. Furthermore, it has been demonstrated that implantation of AAA endovascular stent grafts can be performed safely, and that these devices provide benefits over surgical repair.
Potential risks with this study are minimized by selecting qualified investigators, careful assessment of each subject prior to, during and after implantation. Medtronic has minimized the risks by completing product testing prior to the use of the device in this clinical study, implementing quality control measures into production processes, providing guidelines for subject selection and evaluation, and providing adequate instructions and labeling. However, to date, the DD with SAE potential (transition stent fractures, partial suprarenal stent detachment, suprarenal stent fracture and suprarenal anchoring pin fracture) observations reported have indicated that the Endurant Evo AAA stent graft system has associated risks with higher rates when compared to the associated risks of other commercially available devices.
Because of these findings, there are risks associated with this trial, which are worse than the risks normally associated with the use of the predicate device or other commercially available devices. Therefore, enrollment in the clinical study has been terminated and follow-up for the enrolled subjects will continue.
Risk management for the Endurant Evo AAA stent graft system is performed in accordance with EN 14971:2012 and the results are detailed in the Investigator Brochure.

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L APPENDICES

L.1 Abbreviations

AAA Abdominal aortic aneurysm
ADE Adverse Device Effect
AE Adverse event
ASA American Society of Anesthesiologists ASADE Anticipated serious adverse device effect AUI Aorto-uni-iliac
CEC Clinical Event Committee
CIP Clinical Investigation Plan
CRF Case Report Form
CT Computed Tomography
CVA Cerebral Vascular Incident
DD Device Deficiency
DMC Data Monitoring Committee
EC Ethics Committee
eCRF Electronic Case Report Form
EVAR Endovascular Aneurysm Repair
FDA Food and Drug Administration
F/U Follow-up
IB Investigator Brochure
ICU Intensive Care Unit
IDE Investigational Device Exemption
IFU Instructions for Use
INR International Normalized Ratio
IPR Independent physician reviewer
IRB Institutional Review Board
ISO International Organization for Standardization
KUB Kidney, Ureter and Bladder
MAE Major Adverse Event
MI Myocardial Infarction
MRA Magnetic Resonance Angiography
MRI Magnetic Resonance Imaging
PET Polyethylene terephthalate
PMA Premarket Approval
OD Outer Diameter
SADE Serious Adverse Device Effect
SAE Serious Adverse Event
SOP Standard operating procedure
USADE Unanticipated Serious Adverse Device Effect
WBC White Blood Cell

L.2 Definitions

Major Adverse Events (MAEs)	Definition
All-Cause Mortality	Death from any cause.
Bowel Ischemia	Bloody diarrhea with confirmation via colonoscopy of ischemia or the operative or postmortem demonstration of ischemic changes in the large or small intestine and requires surgical intervention.
Myocardial Infarction	Evidenced on 2 of the 3 following conditions: new clinical symptoms suggesting MI, changes on ECG consistent with MI, and elevated CK > 2 times the upper normal limit (per the normal ranges of the institution).
Paraplegia	Complete loss of motor function in the lower extremities occurring intra- or postoperatively and persisting >1 month.
Procedural Blood Loss ≥ 1000 cc	A blood loss ≥ 1000 cc occurring before the subject leaves the operating room.
Renal Failure	Failure of renal function requiring dialysis.
Respiratory Failure	Need for mechanical ventilation for > 24 hours postoperatively, or re-intubation for anyreason.
Stroke	Development of a new neurological deficit that persists > 24 hours, or worsening of previous neurological symptoms that persist > 24 hours and classified as stroke by a physician.

Secondary Endpoints:	Definition
Aneurysm-Related Mortality	Aneurysm-related mortality is defined as death from rupture of the abdominal aortic aneurysm or from any initial or secondary procedure intended to treat the AAA. If a death occurred within 30 days of any procedures intended to treat the AAA, then it is presumed to be aneurysm-related unless there is evidence to the contrary. Deaths that occurred after 30 days of any procedures intended to treat the AAA that are procedure-related should be aneurysm-related. *Ultimate adjudication of relatedness of death will be made by the Clinical Events Committee (CEC). Excluded are aneurysms in anatomic areas other than the targeted segment treated by the Endurant Evo AAA stent graft system.*
Stent Graft Migration	Stent graft migration can be attributed to migration of the main body stent graft or migration of a stent graft limb/extension. **Main body stent graft migration** is defined as evidence of movement of the main body stent graft relative to fixed anatomic landmarks, which is not due to remodeling of the subject's vasculature. Proximal migration is observed when the stent graft completely covers a renal artery or movement is > 10 mm. Distal migration is observed when the stent graft moves > 10 mm distally relative to fixed anatomic landmarks. **Stent graft limb/extension migration** is defined as evidence of movement of the stent graft limbs/extensions relative to fixed anatomic landmarks, which is not due to remodeling of the subject's vasculature. Proximal migration is observed when the distal part of the stent graft limb/extension moves > 10 mm proximally. Distal migration is observed when the distal part of the stent graft limb/extension moves > 10 mm distally or completely covers the internal iliac artery.
Secondary Procedures	A secondary procedure is defined as any **endovascular** or **surgical**

	procedure performed following the completion of the operative initial implantation procedure (thus on subsequent occasion after final closure of the last artery access site) which involves the targeted vascular segment treated by the Endurant Evo AAA stent graft system, including access sites and bypasses of the targeted vascular segment in which there is either manipulation of the implanted Endurant Evo stent graft or implantation of any additional devices. *(Procedures related to complications due to the use of a closure device are excluded from this definition)*
Aneurysm Expansion	Aneurysm maximum diameter increase >5 mm as compared to the 1- month contrast enhanced imaging measurements
Aneurysm Rupture	Rupture or perforation of the targeted abdominal aneurysmal sac as detected by angiography, CT scan, and/or direct observation at surgery or autopsy. Aneurysm rupture should be reported as either procedure-related aneurysm rupture, (i.e., perforation of the aneurysm during the course of the implantation procedure), or as a late aneurysm rupture that follows device deployment. *Excluded are aneurysms in anatomic areas other than the targeted segment treated by the Endurant Evo AAA Stent graft system.*
Conversion to Open Surgery	Conversion of the endovascular procedure to an open procedure required at the time of the index procedure (primary conversion) or at a time beyond the initial endovascular procedure (secondary conversion).
Major Adverse Events	Major Adverse Events include the occurrence of any of the following: • All-cause Mortality • Bowel Ischemia • Myocardial Infarction • Paraplegia • Procedural Blood Loss ≥1000 cc • Renal Failure • Respiratory Failure • Stroke
Stent Graft Occlusion	Defined as a 100% blockage of the lumen diameter of any implanted the stent graft component(s) as evidenced by CT, angiography, ultrasound, or other appropriate imaging modality, and/or operative or pathological analysis.
Endoleak	Defined by the presence of contrast-enhanced blood outside the lumen of the endoluminal graft but within the aneurysm sac. **Type I** - Endoleak resulting from an incomplete seal of the endograft proximally or distally; the endoleak is in continuity with the proximal anchoring site (proximal endoleak) or the distal anchoring site (distal endoleak) of the device reaching the aneurysm sac. Type I a - Leak at the proximal graft attachment site Type I b - Leak at the distal graft attachment site. Type I c - Leak around an occluding plug **Type II** - Endoleak resulting from a collateral vessel entering the aneurysmal sac resulting in retrograde filling (e.g. inferior mesenteric, middle sacral, hypogastric, accessory renal or lumbar arteries). **Type III** - Endoleak resulting from a defect of fabric or between the segments of the modular graft (junctional endoleak). Type III a – Endoleak between the segments of the modular

	graft (junctional endoleak). Type III b – Endoleak in the mid-graft region due to the defect of fabric **Type IV** – Transgraft leak due to fabric porosity within 30 days after index procedure. **Type V** – Aneurysm enlargement in the absence of any demonstrable perfusion of the aneurysmal sac. **Type undettermined** – Endoleak of undefined origin

Device Deficiency	Definition
Anchoring Pin Fracture	Fracture or breakage of the anchoring pin.
Anchoring Pin Detachment From Aorta	Detachment of the anchoring pin that secures the stent graft to the aorta.
Suprarenal Bare Stent Fracture	Fracture or breakage of the suprarenal bare stent.
Stent Graft Wireform Fracture	Fracture or breakage in stent graft wireform.
Stent Graft Wire Detachment From Fabric	Detachment of the Stent Graft Wire from the fabric.
Suprarenal Bare Stent Detachment from Fabric	Detachment of the Suprarenal Bare Stent from the fabric.
Stent Graft Dilatation	Graft dilatation >50% of the manufacturer's labeled diameter as determined by CT scan, angiography, and/or direct observation at surgery or autopsy.
Stent Graft Extrusion or Erosion	Extrusion or erosion of the metal frame through the full thickness of the vessel wall as determined by CT, angiography, and/or direct observation at surgery or autopsy.
Stent Graft Twisting	Stent Graft obstruction in the vertical plane as determined by CT scan or angiography resulting in an unintentional obstruction (>50%) of blood flow through the vascular lumen not caused by anatomy of the vessel wall.
Stent Graft Kinking	Stent Graft obstruction in the horizontal plane as determined by CT scan or angiography resulting in an unintentional obstruction (>50%) of blood flow through the vascular lumen not caused by anatomy of the vessel wall.
Access Failure	Inability to insert device due to mechanical failure or anatomic exclusions of the femoral or iliac arteries.
Deployment Failure	Deployment failure due to subject anatomy or mechanical failure. This specifically refers to deployment of the stent graft from the delivery system.

Additional Definitions	Definition
Stent Graft Stenosis	Hemodynamically significant (>50%) reduction in the diameter of the stent graft lumen as compared to the reference diameter and not caused by anatomy of the vessel wall.
Stent Graft Infection	The development of a perigraft infection confirmed by direct examination, CT, and/or perigraft aspiration.
Technical Success	Successful delivery and deployment of the stent graft (assessed intra-operatively) in the planned location and with no unintentional coverage of internal iliac arteries or any visceral aortic branches and with the removal of the delivery system.

L.3 Potential Adverse Events

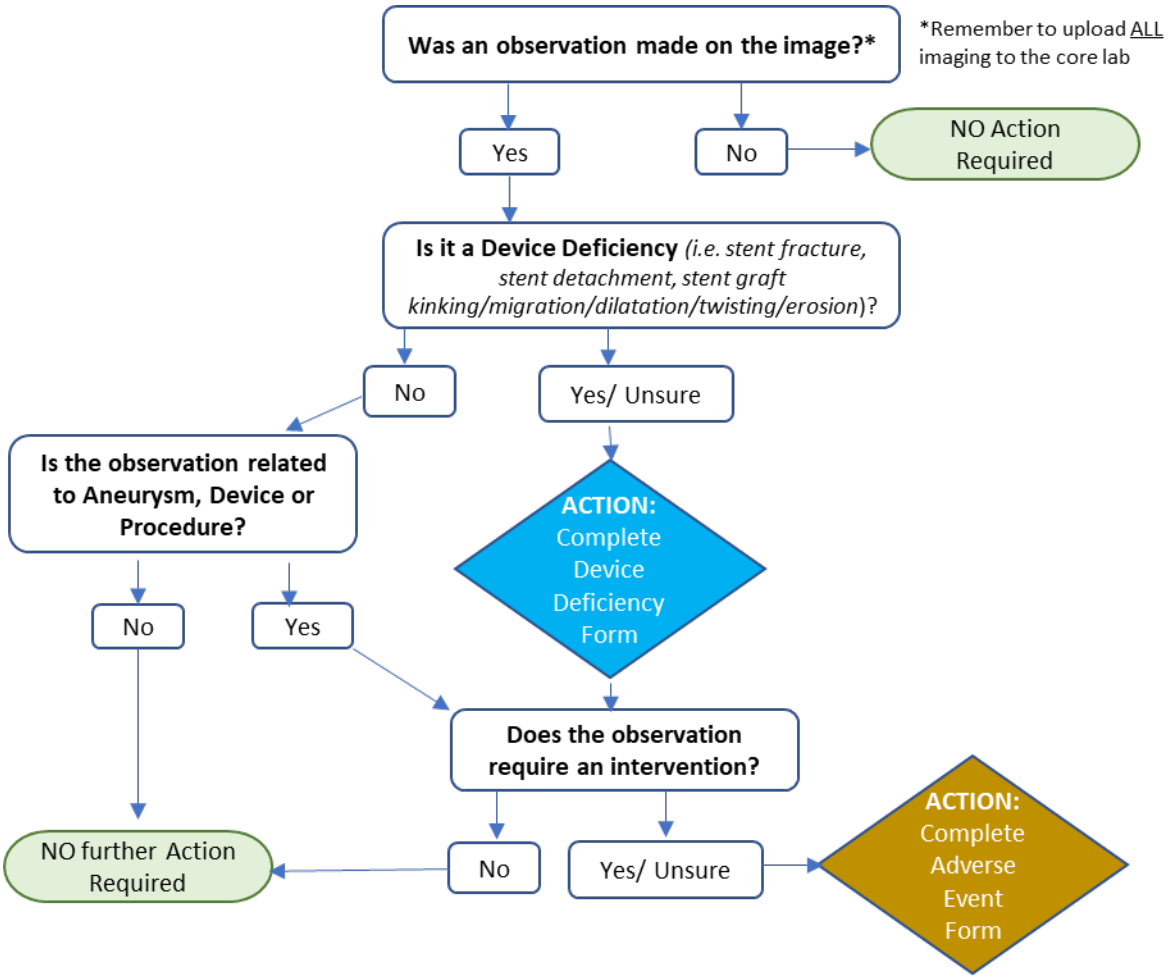
Adverse events that may occur related to the index procedure and/ or device or that require intervention include, but are not limited to, the following:

- amputation
- anesthetic complications and subsequent attendant problems (e.g., aspiration)
- aneurysm enlargement
- aneurysm rupture and death
- aortic damage, including perforation, dissection, bleeding, rupture, and death
- arterial or venous thrombosis or pseudoaneurysm
- arteriovenous fistula
- bleeding, hematoma, or coagulopathy
- bowel complications (e.g., ileus, transient ischemia, infarction, necrosis)
- cardiac complications and subsequent attendant problems (e.g., arrhythmia, myocardial infarction, congestive heart failure, hypotension, hypertension)
- claudication (e.g., buttock, lower limb)
- death
- edema
- embolization (micro and macro) with ischemia (transient or permanent) or infarction
- endoleak
- femoral-femoral artery bypass thrombosis
- fever and localized inflammation
- genitourinary complications and related problems (e.g., ischemia, erosion, fistula, incontinence, hematuria, infection)
- hepatic failure
- impotence
- infection of the aneurysm or device access site, including abscess formation, transient fever, and pain
- lymphatic complications and related problems (e.g., lymph fistula)
- neurologic local or systemic complications and related problems (e.g., confusion, stroke, transient ischemic attack, paraplegia, paraparesis, paralysis)
- occlusion of device or native vessel
- pulmonary complications and subsequent attendant problems
- renal complications and related problems (e.g., artery occlusion, contrast toxicity, insufficiency, failure)
- stent graft: improper placement, incomplete deployment, migration, suture break, occlusion, infection, stent fracture, graft twisting or kinking, insertion and removal difficulties, graft material wear, dilatation, erosion, puncture, and perigraft flow
- surgical conversion to open repair
- vascular access site complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula, dissection
- vascular spasm or vascular trauma (e.g., iliofemoral vessel dissection, bleeding, rupture, death)
- vessel damage
- wound complications and related problems (e.g., dehiscence, infection, hematoma, seroma, cellulitis)

L.4 Imaging Technique and Sensitivity

Anatomy/Stent Graft Issue Detected	CT with contrast	CT without contrast	MRA	MRI	Abdominal X-ray	Duplex CDUS (Ultrasound)	Angiogram/ Aortagram, and Arteriogram
AAA Diameter and Length	1	2	1	2	4	3	3
Stent graft migration	1	2	1	2	3	4	2-3
Stent graft fracture	2	3	2	3	1	4	2-3
Stent graft kinking	2	3	2	3	1	4	2-3
Stent graft twisting	2	3	2	3	1	4	2-3
Stent graft patency	1	4	1	4	4	2	2-3
Endoleaks	1	4	1	4	4	2	2-3
Occlusion	1	4	1	4	4	2	2-3
Stenosis	1	4	1	4	4	2-3	2-3
Stent Graft Fabric Defect	1	4	1	4	4	4	2-3
1= Highly visible	2 = visible	3 = Not very visible (potential artifacts)				4 = Invisible	

L.5 Imaging Device Assessment Reporting Decision Tree



L.6 Table of changes & rationale CIP version 7 compared to version 6

Section	CIP Version 6	CIP Version 7	Rationale for change
Throughout Document	NA	Administrative changes	Correction of previous administrative errors and minor updates
Synopsis	Purpose the purpose of the Endurant Evo International Clinical Trial is to evaluate the safety and effectiveness of the Endurant Evo AAA stent graft system for endovascular treatment of subjects with infrarenal abdominal aortic or aortoiliac aneurysms. The clinical evidence collected as part of this trial is expected to be used to support regulatory approval and subsequent commercialization of the Endurant Evo AAA stent graft system in multiple international geographies. Data collected during this trial may also be used in conjunction with data collected during a concurrently enrolling IDE trial to support PMA approval of the Endurant Evo AAA stent graft system in the United States.	Purpose The purpose of the Endurant Evo International Clinical Trial is to evaluate the safety and effectiveness of the Endurant Evo AAA stent graft system for endovascular treatment of subjects with infrarenal abdominal aortic or aortoiliac aneurysms. ~~The clinical evidence collected as part of this trial is expected to be used to support regulatory approval and subsequent commercialization of the Endurant Evo AAA stent graft system in multiple international geographies. Data collected during this trial may also be used in conjunction with data collected during a concurrently enrolling IDE trial to support PMA approval of the Endurant Evo AAA stent graft system in the United States~~.	
C.1Study objectives	Data collected during this trial may also be used in conjunction with data collected during a concurrently enrolling IDE trial to support PMA approval of the Endurant Evo AAA stent graft system in the United States.	~~Data collected during this trial may also be used in conjunction with data collected during a concurrently enrolling IDE trial to support PMA approval of the Endurant Evo AAA stent graft system in the United States.~~	
E.3 Regulatory Compliance	……The international standard ISO 14155:2011 ('Clinical Investigation of medical devices for human subjects') Medical Device Directive 93/42/EEC laws and regulations of the countries in which the clinical study is conducted, including……	……The international standard ISO 14155:2011 ('Clinical Investigation of medical devices for human subjects') and Medical Device Directive 93/42/EEC will be followed with the following two exceptions: • ISO 8.2.4.5 Routine on-site monitoring visits will be replaced by remote monitoring (see section (G2 and rationale in L5) • ISO6.4.1 Adverse events: Not all adverse events will be collected (see section F6 and rationale in L5) In addition, the study will be compliant with the laws and regulations of the countries in which the clinical study is conducted, including……..	Rationale for the deviation to ISO8.2.4.5 is provided in row G2 of this table) Rationale for the deviation to ISO 6.4.1 is proviced in row F6 of this table)

F.2.3 Follow-Up Visits and Procedures	At all required follow-up visits subjects will undergo the following assessments: •Physical Exam •CT/MR with contrast and non-contrast (2 cm above the origin of the celiac artery through the bifurcation of the femoral arteries) •Abdominal X-ray (4-view, KUB) •EQ5D questionnaire (until 12 months F/U only) •Adverse event assessment •Concomitant Medication	At all required follow-up visits subjects will undergo the following assessments: •Physical Exam (to be reported in FUP eCRF until 24 months only) •CT/MR with contrast and non-contrast (2 cm above the origin of the celiac artery through the bifurcation of the femoral arteries) •Abdominal X-ray (4-view, KUB) •EQ5D questionnaire (until 12 months F/U only) •Adverse event assessment •Concomitant Medication (to be reported in FUP eCRF until 24 months only)	Clinical assessments remain to be done as per site standard of care but it is no longer required to report data from the physical exam and data from concomitant medications from 2 year follow up till the end of the study. In case of medications administrated for reportable adverse events the medications should be added in the description of the event if relevant
F.3 Data Collection Requirements	Imaging source data will be sent to a Core Lab for analysis up to the 60-month follow-up visit. Any interim imaging of the stent graft region but not linked to a study visit should be recorded on the Interim Image e-CRF (e.g. imaging performed as standard of care beyond the protocol required time points and/or when performed further to any issue observed at previous imaging Follow-up). Interim imaging performed, as recommended per the most recent DMC Surveillance and Management letter should also be reported on the interim imaging eCRF. Study data will be collected using electronic case report forms (eCRFs) as described in Section G.1. Clinical investigators must electronically review and approve all eCRFs. Medtronic monitors will perform source document verification of the eCRFs. The monitoring strategy will be defined in the monitoring plan. For test equipment critical for assessing endpoints (e.g., CT scan, Duplex Ultrasound, x-ray) maintenance and calibrations will be monitored periodically.	Imaging source data will be sent to ~~a~~ the Core Lab for analysis up to the 60-month follow-up visit. Any interim imaging of the stent graft region but not linked to a study visit should also be ~~recorded on the Interim Image e-CRF~~ sent to the Core Lab (e.g. imaging performed as standard of care beyond the protocol required time points and/or when performed further to any issue observed at previous imaging Follow-up). This also includes interim imaging performed as recommended per the most recent DMC Surveillance and Management letter. ~~should also be reported on the interim imaging eCRF.~~ All images taken from the stent graft region must be assessed by the site. Any findings that meet the requirements in the flowchart (Appendix L.8) must be reported on the applicable eCRF. Study data will be collected using electronic case report forms (eCRFs) as described in Section G.1. Clinical investigators must electronically review and approve all eCRFs. ~~Medtronic monitors will perform source document verification of the eCRFs.~~ The monitoring strategy will be defined in the monitoring plan. ~~For test equipment critical for assessing endpoints (e.g., CT scan, Duplex Ultrasound, x-ray) maintenance and calibrations will be monitored periodically.~~	In protocol version 6, images were analyzed by both Core Lab and sites. Moving forward, protocol version 7 will continue to require that the sites submit all images to the Core Lab for analysis, but the sites will not be required to report all data from imaging analysis. This is because the Core Lab will assure consistency between measurements of different sites. In addition, there is a discrepancy between the number of Device Deficiencies identified by the Core Lab and Sites. The Core Lab has proven more reliable at identifying Device Deficiencies as compared to the sites. For this reason, the Core Lab has demonstrated to be the most accurate and reliable data source for the image analysis. If in an incidental case, the site identifies a device deficiency that is not confirmed by the Core Lab, this finding will still be captured as the site continues to report such findings in the device deficiency or event eCRFs. For this reason, the decision to relieve sites from also entering this data into eCRF is not expected to affect overall data integrity. See section G.2 Monitoring Procedures on details regarding the monitoring process.

F.3 Data Collection Requirements Table F2 Data Collection Schedule	**Last column** **2-5 Yr. FU (±56 days)** • Physical examination • Medications • Adverse Event Assessment • CT/MR (2 cm above origin of celiac artery through bifurcation of femoral arteries) [c] • Abdominal X-Ray (4-view, KUB)	**Last column** **2~~-5~~ Yr. FU (±56 days)** • Physical examination • Medications • Adverse Event Assessment • CT/MR (2 cm above origin of celiac artery through bifurcation of femoral arteries) [c] • Abdominal X-Ray (4-view, KUB) **Column added** **3-5 Yr. FU (±56 days)** • Adverse Event Assessment • CT/MR (2 cm above origin of celiac artery through bifurcation of femoral arteries) [c, f] • Abdominal X-Ray (4-view, KUB)[f] **Footnote added** [f] All Images (routine & interim) performed 3-5 years will be required to be submitted to the Core Lab for evaluation. Sites will continue to review images for clinical evaluation and detection of device deficiencies in accordance with Appendix L.8, but will not be required to complete imaging eCRF.	Changes detailed in sections F.2.3 and F.3 are implemented in table F-2: schedule of assessments
F.6. Adverse Events Recording and Reporting of Adverse Events	For the purpose of this clinical investigation Medtronic will define and classify the following events per ISO14155:2011 and Title 21 CFR part 812.3.	For the purpose of this clinical investigation Medtronic will define and classify the following events per ISO14155:2011 (followed for definitions of Adverse Events only) Adverse event reporting for the remaining follow up (3-5 years) will focus on the reporting of the below listed events: • Adverse events with a possible, probable or causal relationship to the aneurysm (Excluding aneurysms in anatomic areas other than the Endurant grafted segment) • Adverse events with a possible probable or causal relationship to the device • Adverse events with a possible probable or causal relationship to the index procedure • Adverse events leading to subject's death Secondary procedures performed as a result of any of the above adverse events must	Because the Modular PMA was withdrawn, it was decided to focus on the collection and review of safety follow-up data for which the relationship to the aneurysm, device or procedure cannot be ruled out, for the remainder of the follow up period. This means that Medtronic will no longer require the reporting of events unrelated to the aneurysm, device, or procedure. This decision was deemed appropriate as the DMC has not reported any concerns with regards to events with no relationship to aneurysm, device or procedure. If a relationship cannot be ruled out, sites are requested to report the event. To aid the sites in making a decision on reporting, an additional guidance flowchart was added in the protocol.

		be reported on the respective Adverse Event form. Please see guidance for reporting of adverse events following image review in Appendix L.5.	
F.6.2 Adverse Events Recording and Reporting of Adverse Events	Adverse Event (AE) information will be collected throughout the study and reported to Medtronic on the Adverse Event eCRF. All Adverse Events (except the ones listed in table F-3), regardless of relatedness or outcome, must be reported. The investigator is responsible for reporting all AE to Medtronic. See the Adverse Event eCRF for the information to be reported for each Adverse Event.	Adverse Event (AE) information will be collected throughout the study and reported to Medtronic on the Adverse Event eCRF. ~~All Adverse Events (except the ones listed in table F-3), regardless of relatedness or outcome, must be reported.~~ The investigator is responsible for reporting all AEs as reportable/collectable per CIP to Medtronic. See the Adverse Event eCRF for the information to be reported for each Adverse Event. Please see guidance for reporting of Adverse Events following image review in Appendix L.5.	
F.6.3 Adverse Events Recording and Reporting of Device Deficiencies		**added at the end of the section:** Please see guidance for reporting of Device Deficiency following image review in Appendix L.5.	
L.5 Imaging Device Assessment Reporting Decision Tree	NA	**Added:** Imaging Device Assessment Reporting Decision Tree.	
G.2. Monitoring Procedures	Monitoring visits will be conducted at the start, during and at the closure of the clinical study in accordance with Medtronic SOPs and the Monitoring Plan. Frequency and timing of monitoring visits shall be determined by the Sponsor for each site based on enrollment rate and volume, study compliance and findings from previous visits.	On-site monitoring visits will be conducted at the start and during ~~and at the closure of~~ the clinical study in accordance with Medtronic SOPs and the Monitoring Plan. Frequency and timing of monitoring visits shall be determined by the Sponsor for each site based on enrollment rate and volume, study compliance and findings from previous visits. (…) In-person monitoring visits will be replaced by telephone and email contact to the sites by the study team. The sponsor monitoring phone calls will include an assessment of the source documents to assure completeness of image submissions and event reporting and an assessment of the essential documents. In particular, the focus of these calls will be to ensure that safety data is entered and to verify that all relevant events are reported. Site monitoring visits will be	To further mitigate the concern that sites could underreport safety events, it is noted that the following two procedures will remain to be in place: First, all sites will still be required to submit all images to Core Lab for analysis. The Core Lab will continue to analyze all site images for potential device deficiencies or other notable findings. Second, Medtronic will continue to monitor all source data received from the sites for any potential unreported adverse events (i.e. source data from adjudicable adverse events or source data requested by the DMC). Any findings from these additional verification procedures will be addressed with the site.

		requested by the Sponsor if a concern arises with regards to compliance or data integrity.	
G.4. Study Close Out	Prior to completion of study close out, all data must be entered and monitored in the EDC system. Medtronic and/or its designees will notify the site of the intention to close the study. Study close out visits may be performed. During these visits, the monitors will ensure that the investigator's regulatory files are up to date and complete and that any outstanding issues from previous visits have been resolved.	Prior to completion of study close out, all data must be entered and ~~monitored~~ approved in the EDC system. Medtronic and/or its designees will notify the site of the intention to close the study. Remote s~~S~~tudy close out visits may be performed. ~~During these visits, the monitors will ensure that~~ The intent of these visits will be to assure that the investigator's regulatory files are up to date and complete and that any outstanding issues from previous visits have been resolved.	
J. 3 Risk-to-benefit Rationale	However, to date, the UADE (transition stent fractures, partial suprarenal stent detachment, and suprarenal stent fracture) observations reported have indicated that the Endurant Evo AAA stent graft system has associated risks with higher rates when compared to the associated risks of other commercially available devices.	However, to date, the UADE (transition stent fractures, partial suprarenal stent detachment, ~~and~~ suprarenal stent fracture, and suprarenal anchoring pin fracture) observations reported have indicated that the Endurant Evo AAA stent graft system has associated risks with higher rates when compared to the associated risks of other commercially available devices.	Text updated to include the new UADE, suprarenal anchoring pin fracture, to already listed UADEs in the previous version of the protocol.
L.6 table of changes		Added table of changes CIPv7 versus CIPv6	