Investigational Device Exemption G 010002

Endovascular Exclusion of Thoracoabdominal Aortic Aneurysms or Abdominal Aortic Aneurysms Utilizing Fenestrated/Branched Stent-grafts

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APPENDIX A: INFORMED CONSENT

APPENDIX B: CASE REPORT FORMS

APPENDIX C: RELEVANT PUBLICATIONS

APPENDIX D: DEVICE DESCRIPTIONS

1) Report of Prior Investigations/Background

Endovascular repair of abdominal aortic aneurysms has become the dominant form of treatment for anatomically suitable patients. Yet limitations to the technique are multiple and primarily relate to the complex morphologies of some aneurysms. Although improvements of stabilizing features have been made, such as suprarenal stenting and the use of barbs, a segment of proximal and distal artery must adequately appose to the graft material and create a seal (defined as the neck). In the absence of an adequate amount of infrarenal neck, we are unable to create an adequate proximal seal between the prosthesis fabric and the aortic wall to exclude the aneurysm from systemic pressures if conventional devices are employed. Most endovascular devices require a minimum of 15 mm of proximal neck below the renal arteries to ensure aneurysm exclusion. Although recent devices have been advocated for use in shorter necks (< 15mm), none have reported successful long-term outcomes. Furthermore, data from the EVAR trails at 10 years indicates that the stability of repairs in the setting of complex anatomy is questionable at best. Prior devices that had been marketed for short proximal necks had significant complications, and post hoc analyses of studies as well as post market data have resulted in a revision of the guidelines to utilize the graft only in patients with necks lengths greater than 15mm (AneurRx). Other strategies rely upon columnar support to mitigate the need for fixation and sealing in the aorta around the renal arteries. The later grafts are stiff graft and contain longitudinal support structures in an effort to prevent migration. Such devices are intended to “stand up” within the iliac arteries. However, the applicability of rigid columnar support in the setting of aortic or iliac tortuosity is not valid. Consequently, it seems only logical for clinicians to strive to define a region of healthy vessel above and below the diseased (aneurysmal) artery to provide durable fixation and sealing. Following the identification of such regions, the area intended to be excluded should then be inspected for arterial branches that supply critical organs with arterial blood, and those arteries must be incorporated into the repair. This is the basis for fenestrated and branched aortic grafts.

Open surgery has been employed for such aneurysms using techniques including supravisceral segment clamping, reimplantation of visceral arteries, and cardiopulmonary bypass. However, in healthy surgical candidates at centers of excellence carry mortality rates of 10% or greater. Statewide medicare audits estimated mortality for such procedures to be 19% at 30 days and 31% at 12 months. Other complications, including respiratory, cardiac, renal and neurologic are frequent. Many patients, particularly those over 70-75 years of age are never offered surgical repair and do not undergo aneurysm treatment. Thus, the advent of endovascular technologies that result in a lower incidence of the aforementioned complications will allow the treatment of patients that historically have no surgical option, or in healthier patients diminish the exceptionally high surgical risks.

2) Investigational Plan

a) Purpose

i) Intended Use

The purpose of the study is to evaluate the role of fenestrated/branched stent-grafts in the exclusion of abdominal aortic aneurysms involving critical branches, thoracoabdominal aortic aneurysms, iliac aneurysms, renal artery aneurysms [S45] and SMA aneurysms [S207]. The evaluation shall be conducted with subjects considered to be "high-risk", thus would be at risk for developing complications following open surgical repair. Patients will be grouped in accordance with the anatomic extent of the aneurysm intended to be treated as follows:

1) Patients with infrarenal or iliac disease in the presence of an infrarenal neck ≥ 3 mm distal to the lowest renal artery are considered to have a juxtarenal aneurysm.

2) Patients with aneurysms involving the origin or actual branch vessel including of the renals, superior mesenteric, or celiac arteries are considered to have a thoracoabdominal aneurysm.

3) Patients with aneurysms involving the iliac artery or arteries in addition to an aneurysmal aortic segment are considered to have aortoiliac aneurysms potentially in addition to one of the two previous categories.

The sealing zones of the device will exist proximal to the most cranial extent of the aneurysm and distal to the most distal extent of the aneurysm intended for treatment. Given that each of the three anatomic categories of patients will have markedly different expected outcomes when surgical procedures are utilized, they will be separately analyzed from the endovascular standpoint. The methods by which the critical branches will be incorporated will include fenestrations and side-arm branches. Please see section 2d and Appendix D for more detailed information

ii) Objectives

The primary objective of the study is to assess the safety of the fenestrated/branched endovascular prosthesis in the prevention of aneurysm rupture in patients considered high-risk for open surgical repair. Secondary analyses include an assessment of the risks associated with fenestrated/branch repairs with respect to cardiac, pulmonary, renal, neurologic and other complications.

iii) Duration

The duration of the investigation shall include a two year follow-up period for subjects that were treated with a fenestrated/branched endograft in a staged fashion or whose graft construction included a low-profile system including both nitinol stents and low-profile graft material. Subjects shall be evaluated at pre-operative, operative, prior to hospital discharge, one, six (if considered medically necessary), twelve and twenty-four months. Subjects will be encouraged to continue follow-up thereafter given that the presence of extensive aneurysmal disease emphasizes the benefit of follow-up for the repaired segment as well as other regions of the arterial system that may be at risk for late

degeneration. Remaining patients will be offered clinical follow up for the completion of the study with no data collection.

b) Protocol

i) Study Design

This study will be a prospective, non-randomized evaluation of endovascular aneurysm repair with fenestrated/branched devices in high-risk patients.

ii) Inclusion Criteria

Patients will be considered suitable if they fulfill all of the Inclusion Criteria, which includes both general and anatomic criteria. General inclusion criteria will be assessed during the initial patient evaluation. Anatomic criteria will be assessed using a variety of imaging techniques that are routinely performed during the evaluation of abdominal aortic aneurysms.

General:

1) At least 18 years of age

2) Not pregnant

3) Willing and able to comply with two-year follow-up period

4) Willing and able to give informed consent prior to enrollment

- In case of urgent repair with a standard p-Branch device only, patient (if capable) or family member are acceptable to provide informed consent prior to treatment[S229]

5) No known allergy to stainless steel, nitinol, or polyester. For patients getting a Low-Profile device they may have an allergy to stainless steel as this is not a component of those grafts constructions[s306].

6) No history of anaphylactic reaction to contrast material with an inability to properly prophylax the patient appropriately.

7) Life expectancy greater than two years (except for p-Branch protocol for ruptured aneurysms)

8) High risk candidate for open surgical repair

9) Presence of at least one of the following aneurysms is necessary to drive the need for a repair with a fenestrated/branched device:

i) An abdominal or thoracoabdominal or aortic aneurysm ≥ 4 cm or suggestive of a high risk of rupture as a result of morphology, growth history or symptoms

ii) An Iliac aneurysm > 35 mm or suggestive of a high risk of rupture as a result of morphology, growth history or symptoms

iii) A renal artery aneurysm > 20 mm (or twice the diameter of native renal artery) [S45]

iv) An SMA aneurysm >30 mm [S207]

Subsequent anatomic inclusion criteria refer to the anatomic extent of disease for the given patient.

I. Juxtarenal Aneurysms treated with Fenestrated devices (Subjects must meet ALL of the Anatomic Inclusion Criteria)

1) Proximal neck length below distal most visceral artery to remain patent ≥ 3 mm and ≤ 15 mm in length[S# 322]

2) Proximal neck diameter ≤ 32 mm

3) Proximal neck angulation ≤ 80°

4) Iliac artery diameter ≥ 7 mm (anticipated diameter following balloon angioplasty, stenting, dottoring, or conduit) or ≥ 6 mm for patients receiving a Low-Profile device[s306].

5) Iliac angulation that will not preclude device delivery or surgical modification of the iliac system

6) For a bifurcated or aorto-monoiliac prosthesis, the iliac implantation site(s) are ≤ 20 mm in diameter and ≥ 20mm in length

7) For a straight aorto-aortic prosthesis, distal neck (normal aorta between the aneurysm and iliac bifurcation) ≥ 15 mm in length and ≤ 32 mm in diameter

8) If a hypogastric branch will be used to treat the common iliac aneurysm [S34, S145, S232]:

a) the intended common iliac artery is > 20mm in diameter or the aneurysm has morphology concerning for rupture; and

b) the intended distal fixation site within the internal iliac is ≤ 10mm in diameter.

9) Renal arteries or other visceral vessels arising from the aorta in an orientation that is evident and measurable from cross-sectional imaging (CT or MR)

II. Thoracoabdominal aneurysms treated with Fenestrated/Branched devices: (Subjects must meet ALL of the following)

1) An absence of adequate aortic neck (≥ 3mm) below one or more critical aortic branches requiring a seal to be created above the lowest critical branch with a mating stent-graft designed in accordance with the use of reinforced fenestrations or side arm branches.

2) Proximal neck diameter ≤ 40 mm and proximal neck length ≥ 10mm

3) Iliac artery diameter ≥ 7 mm (anticipated diameter following balloon angioplasty, stenting, dottoring, or conduit) or ≥ 6 mm for patients receiving a Low-Profile device[s306].

4) Iliac angulation that will not preclude device delivery or surgical modification of the iliac system

5) For a bifurcated or aorto-monoiliac prosthesis, iliac implantation sites require ≤ 20 mm in diameter and ≥ 20 mm in length

6) For a straight aorto-aortic prosthesis, distal neck (normal aorta between the aneurysm and iliac bifurcation) ≥ 10 mm[S238] in length and ≤ 40 mm in diameter

7) If a hypogastric branch will be used to treat the common iliac aneurysm [S34, S145, S232]

a) the intended common iliac artery is > 20mm in diameter or the aneurysm has morphology concerning for rupture; and

b) the intended distal fixation site within the internal iliac is ≤ 10mm in diameter.

8) Renal arteries or other visceral vessels arising from the aorta in an orientation that is evident and measurable from cross-sectional imaging (CT or MR)

9) Visceral branch diameters (for incorporated vessels) between 4 mm - 11 mm at the intended distal sealing site (thus distal to a visceral artery aneurysm in such circumstances).

10) > 5 mm of proximal visceral branch length to allow for a seal with the mated device, or the ability to exclude an early branch.

A standardized branched device (p-Branch) may be used in place of custom Fen/Branch device if the patient meets criteria p-branch designs options A or B as defined below.

III. Specific Anatomic Inclusion Criteria for Standard p-Branch:
(Subjects must meet ALL of the anatomic criteria in Option A or ALL of the anatomic criteria in Option B[S207]; for ruptured or symptomatic aneurysm, see Option C[S235]).

A. Pivot Fenestration Option A (renal fenestrations come off at same longitudinal level)

1) The celiac artery arises from the aorta between 11:30 – 1:30 with respect to the SMA position (20mm wide scallop that is 20mm deep).

2) The SMA is ≥ 11 mm distal to the celiac artery (unless the celiac artery is occluded or expendable).

3) Longitudinal positions of renal arteries arise 4.5 mm – 19.5 mm distal to the SMA.

4) Radial measurements are calculated based on a clock position of the SMA at 12:00. The circumferential location of the right renal can range from 8:30 – 10:30 and the circumferential location of the left renal artery can range from 1:30 – 3:30 based on an assumed aortic stent graft diameter of approximately 30 mm.

B. Pivot Fenestration Option B (left renal fenestration lower longitudinally than right)

1) The celiac artery arises from the aorta between 11:00 – 2:00 with respect to the SMA position (30 mm wide scallop that is 16mm deep).

2) The SMA is ≥ 9 mm distal to the celiac artery (unless the celiac artery is occluded or expendable).
3) Longitudinal position of the right renal artery arises 8.5 mm – 23.5 mm distal to the SMA.
4) Longitudinal position of the left renal artery arises 12.5 mm – 27.5 mm distal to the SMA.
5) Radial measurements are calculated based on a clock position of the SMA of 12:00. The circumferential location of the right renal can range from 8:30 – 10:30 and the circumferential location of the left renal artery can range from 1:30 – 3:30 based on an assumed aortic stent graft diameter of approximately 30 mm.

Rotational Option for Options A and B: The clock position of the right pivot fenestration is equivalent to the SMA fenestration's clock position minus 1 1/2 to 3 1/2 hours. Thus if the SMA is at 1:00 vs. 12:00, the location of the right renal artery can arise at 9:30 - 11:30 vs. 8:30 - 10:30 and still be accommodated with this option, providing the longitudinal measurements' criteria are met.

The circumferential location of the left pivot fenestration is equivalent to the SMA fenestration's clock position plus 1 1/2 to 3 1/2 hours. Thus if the SMA at 1:00 vs. 12:00, the location of the left renal artery can arise 2:30 - 4:30 vs. 1:30 - 3:30 and still be accommodated with this option, providing the longitudinal measurements' criteria are met.

C. In the setting of a need for an urgent repair for ruptured or symptomatic aneurysm using a standardized p-branch device, the following criteria will be used for inclusion*:

If the proximal neck has angulation <60 degrees (allowing for longitudinal repositioning of the device as the renals are cannulated), the range on the renal arteries is increased by one radius (7.5 mm) of the pivot fenestration. In this light the renals will be as follows:

Option A: Longitudinal positions of renal arteries arise: 3 mm proximal to the SMA to 27 mm distal to the SMA.

Option B: Right renal: arises 1 mm to 31 mm distal to the SMA. Left renal: 5 mm to 35 mm distal to the SMA.

* Note: In certain situations, one may elect to occlude one of both renal arteries to allow for repair to be accomplished.

The documentation of the inclusion criteria is located in subject's study binder.

iii) Data Points

Data will be collected prospectively and recorded. Case report forms (CRFs) will be kept electronically in a database (OmniComm Clinical software [R042]). The case report forms allow for an extensive collection of data, some of which is pertinent to the study (white regions) and other portions are not relevant to the study (grey regions) but which may be useful for analysis of other outcomes. The CRFs include regions that are shaded grey (data that is not required for all enrolled patients) and unshaded segments (white) which includes data pertinent to the study analysis.

Preoperative Imaging: The choice of axial imaging technique will be left up to the ordering physician. However, a cross-sectional imaging study is mandatory, while angiography and intravascular ultrasound will be performed selectively as is currently done prior to infrarenal abdominal aneurysm repair.

Follow-up Imaging: The results of the endovascular repair will be assessed by radiologic and/or clinical criteria at the time of graft placement, prior to hospital discharge, and at follow-up approximately 1, 6 (optional [S128]), 12 and 24 months post implantation, according the imaging schedule listed below. Follow-up studies of devices that are primarily constructed of stainless steel will include CT imaging. Nitinol devices that provide acceptable signal-voids with MRI studies can be imaged with that modality.

Imaging Schedule for IDE G# 010002:

	Pre-op	Intra-op	Prior to d/c	1 month	6 month	12 months	24 month	Yearly Surveillance
CT Scan	X[A]		X[B]	X[B]	X[C]	X	X	X[D]
Angiography	X[A]	X						
KUB			X[B]	X[B]	X[C]	X	X	X[D]
Ultrasound			X[B]	X[B]	X[C]	X	X	X[D]

A) Angiography will be performed selectively. MR may be substituted depending on physician preference

B) These studies may be obtained prior to hospital discharge or within the 1 month follow-up window [S187]

C) 6 month studies are optional and generally indicated in the presence of a concerning endoleak, or other factor that may warrant further evaluation [S128]

D) Long term follow up (beyond 24 months) is not part of the study protocol. Studies, following the initial 24 months, may be obtained

Preoperative Data:

Data will be collected and stored in a database. The case report forms (CRFs) contain the information which we will be collecting. In summary the focus of the data collection includes but is not exclusive to:

1) Physical Exam

2) Past Medical and Surgical History

3) Family History

4) Lab values

5) Pulse Evaluation or ABI [S6]

6) Current Medications

7) Imaging studies

Intraoperative Data:

Data will be collected and stored in a database. The case report forms (CRFs) contain the information which we will be collecting. In summary the focus of the data collection includes but is not exclusive to:

1) Date of Procedure

2) Significant Times during procedure

3) General Anesthesia Records

4) Device information

5) Details on Additional Procedures

6) System Evaluations

Pre-discharge Data:

The interval between deployment of the endoprosthesis and discharge from the hospital will be documented. The case report forms (CRFs) contain the information which we will be collecting. In summary the focus of the data collection includes but is not exclusive to:

1) Date of Discharge

2) Physical Exam

3) Lab values

4) Incisional Status

5) Pulse Evaluation or ABI [S6]

6) Assessment of Adverse Events

7) Relevant Imaging Studies

Follow-up Data:

The case report forms (CRFs) contain the information which we will be collecting. In summary the focus of the data collection includes but is not exclusive to:

1) Date of Examination

2) Physical Exam

3) Lab values

5) Pulse Evaluation or ABI [S6]

6) Assessment of Adverse Events

7) Imaging Studies

Deaths:

Details of any deaths occurring during the evaluation will be stored in a database. The case report forms (CRFs) contain the information which we will be collecting. In summary the focus of the data collection includes but is not exclusive to:

1) Date of Death

2) Cause of Death (if available)

3) Whether or not the Death was Device or Procedure Related

4) Whether or not the Death was Related to a Previous Condition

5) Whether or not an autopsy was performed

Explants:

Attempts will be made to obtain an autopsy in all patients who die at the treating center with prosthesis in place. If possible, at the autopsy, the entire abdominal aorta will be excised – from the celiac axis down to and including both common iliac arteries. The specimen will undergo histologic examination and be sent to the manufacturer to for further evaluation.

Data will be collected and stored in a database. The case report forms (CRFs) contain the information which we will be collecting. In summary the focus of the data collection includes but is not exclusive to:

1) Date of explant

2) Patient's status at explant

3) Reason for explant

Loss to Follow-up or Patient Withdrawal:

If a patient is lost to follow-up or decides to withdraw, data collected is stored in a database. The case report forms (CRFs) contain the information which we will be collecting. In summary the focus of the data collection includes but is not exclusive to:

1) Date of last contact with patient

2) Reasons for patient's unavailability: withdrawal, moved away, unreachable, and so forth

3) Summary of attempts to contact patient

iv) Stentgraft sizing

Grafts may be custom made for each patient or utilize a standard design (p-branch) is chosen based on the findings from preoperative radiologic studies, including computerized tomography, magnetic resonance imaging, and possibly conventional angiography. Rarely will one patient have anatomy amenable to the use of a customized graft of another patient, but should measurements coincide, then the devices may be used accordingly.

Stent-graft Diameter

The diameter of the graft is generally 10 to 20 percent larger than the intended proximal implantation site. The attachment site for distal implantation is oversized by 5 to 15 percent. The assumption being that a small amount of graft redundancy would be inconsequential, whereas, as small deficiency in the diameter of the graft would result in either endoleakage or graft migration.

Determination of proximal graft diameter depends primarily on a measurement of the aneurysm neck from reconstructions based upon CT data. Centerline of flow analyses are the current preferred method for sizing and planning, but in some circumstance and historically (when such techniques were not readily available) axial images were assessed. In the setting of an elliptical appearance of the aorta axial images, the true profile may be assumed to be circular, and the true diameter is more closely approximated by the diameter of the narrowest part (short axis) of the ellipse.

Stent-graft Length

Given the tension of the graft on the delivery system at the time of distal stent implantation, it is assumed that the graft will take the shortest path available from proximal to distal. The primary imaging modality used to determine the length of the graft will vary depending on the tortuosity of the aorta and the availability of multiplanar reconstructions, surfaced shaded displays, centerline of flow analyses and other representations of spiral CT, MR data, or angiographic images.

Sizing for fenestrations and branches

Visceral vessel anatomy and relative orientation adds a level of complexity to endovascular repair of aortic aneurysms. The majority of this will be accomplished from data obtained from spiral CT scans. Important characteristics include the relationship of the renal arteries, the distance between them and the superior mesenteric artery, as well as the relationship between the celiac and superior mesenteric artery. The radial orientations of the aortic branches are expressed as clock positions assuming noon to be the most anterior location on the aorta. These will be assessed using cross-sectional images or centerline of flow reconstructions when available. In general, fenestrations will be placed as closely as possible to the target vessel, while sidearm branches will terminate 1-2 cm above or below the target branch (downward and upward going branches respectively). Pivot fenestrations are intended to have the larger circumference overlap with the target branch.

v) Statistical Analysis

The subject data will be collected and descriptive statistics shall be preformed to assess safety. Mortality will include all-cause mortality and aneurysm related mortality analysis. The latter is defined by any death within 30 days of the index procedure, secondary intervention, or death related to the target aneurysm repair. Given the absence of a comparison group (control group), there is no definitive cutoff point describing safety or efficacy for the study. Instead, the data with respect to mortality, and other complications, will be tabulated throughout the 2 years of the study, and over longer follow-up durations when data is available. Data will be tabulated and submitted to the FDA as part of the annual progress report.

vi) Implant Procedure Description

The procedure will be performed in the operating room under local, epidural, or general anesthesia depending on patient factors. The patient will be positioned on a radiolucent operating table to permit fluoroscopic examination of the entire abdomen and groins. A high-resolution digital imaging system is required to guide placement. Several publications have described the various implantation techniques in detail. The fundamentals of the procedures are highlighted here with respect to the method by which the branch artery will be incorporated:

1) Conventional fenestration device: the visceral segment of the graft is deployed and aligned with the target arteries. Access into the aortic graft from an alternative site (contralateral femoral, iliac, or brachial) is achieved, and the target fenestration is selectively cannulated. The target visceral vessel is then cannulated through the fenestration, and a reasonably stiff wire is placed into the fenestration. A sheath is advanced into the target artery,

and the mating stentgraft is positioned within the sheath to join the target artery with the aortic stentgraft such that 3-4mm of the mating stentgraft protrudes into the aorta. The sheath is withdrawn, and the mating stentgraft is deployed on a balloon sized to the target artery. A larger balloon is then used to flare the proximal (aortic) component creating a rivet like seal. This is repeated for each fenestration, and then the required mating components are inserted to mate with the visceral component to complete the repair.

2) Preloaded fenestrated device: In this situation, one or more fenestrations are preloaded with a wire that transcends the delivery system. Preloaded fenestrations can be accessed in a conventional manner (as above) or with the use of the preloaded wire (ipsilateral to the main device). In the later situation, a sheath is advanced over the preloaded wire and positioned near the target fenestration after the aortic component is oriented and partially deployed. A second catheter and wire within the sheath is then used to access the target vessel. Once all of the target vessels have been cannulated, the preloaded wire is removed and the sheath is advanced over a wire into the target artery. The mating stentgraft is deployed as described above. This is repeated for each fenestration, and then the required mating components are inserted to mate with the visceral component to complete the repair.

3) Side-arm branches: Generally one or more of the side-arm branches have preloaded wires. This is retrieved from an alternative access site, and a sheath is advanced from that location over the preloaded wire into the target branch. A second catheter and wire is then used to cannulate the target vessel from within the branch, and a stiff wire is introduced. The sheath is advanced into the branch if necessary (requiring removal of the preloaded wire) or a mating self-expanding or balloon-expandable stentgraft delivery system can be advanced into the target artery. The mating stentgraft is deployed and ballooned if necessary. This is repeated for each branch, and then the required mating components are inserted to mate with the visceral component to complete the repair.

4) Fenestrations and side-arm branches: In some instances in which the graft design incorporates both fenestrations and side-arm branches, pre-loaded wires simultaneously incorporate both a fenestration and side-arm branch [S306]. These designs are utilized as outlined above with the fenestration being accessed as a preloaded fenestration and the side-arm branch being accessed from a remote vessel as a preloaded branch.

Grafts may be inserted from either femoral artery with consideration given to the degree of tortuosity and occlusive disease noted from preoperative imaging techniques, and adjunctive iliac procedures include, but are not limited to, angioplasty, stenting, stentgrafting or conduit placement. Patients are anticoagulated during the procedure, and when available activated clotting times are used to monitor the anticoagulation intermittently throughout the procedure. Angiography, selective arterial catheter placement or fusion imaging techniques may be used to help locate the visceral arteries. Correct positioning of the prosthesis depends on the relationship of the imaging system to the patient. The aortic visceral component is advanced to bring the metallic stents to the desired location. The position of the graft, as indicated by the position of the proximal and distal stents, can be modified during deployment by manipulation of the delivery system. Once the proximal aspect of the graft is in the appropriate location, markers on the fenestration of the graft would be aligned with the orifice of the visceral vessel to be treated. The graft is then partially deployed. Because of the proximal and distal fixation of

the endograft to the delivery device, the whole system can be rotated, or realigned with the visceral vessel, after partial deployment. The fenestrations or branches are then mated with the target artery as described above. Following access into each of the target arteries, the aortic component is allowed to expand fully by removal of the constraining wires. Several different possible designs exist, thus some flexibility in the deployment sequence is allowed and may be customized for each patient. The proximal (when necessary) and distal portion (potentially using additional components) is then completed. These include thoracic grafts, aortic cuffs, distal bifurcated components, hypogastric branch components, or customized one-piece designs with the bifurcation portion of the device incorporated into the fenestrated/branched portion. Additional stents or stentgrafts may be required to ensure adequate end-organ perfusion and the elimination of sac pressurization and endoleaks.

In certain situations, there may be a need to block off a fenestration in the prosthesis following implantation. This can occur in one of two circumstances:1) planned - in the setting of a ruptured or symptomatic aneurysm where an off-the- shelf device is utilized and the patient has only one kidney that can be incorporated into the repair, the non-relevant fenestration may be required to be occluded.
2) unplanned - in the setting of an inability to cannulate the target artery after the fenestration is cannulated, the fenestration may be required to be occluded. (note: this is considered to be a technical failure in such a case).

Occlusion of a fenestration is accomplished using different methods. When the fenestrations are longitudinally disparate, a conventional aortic extension may be used to cover a fenestration. If that is not possible a modification to a covered branched stentgraft (Atrium or Jomed) may be used. In this manner the balloon expandable stent is placed over a wire that is through the fenestration, but not in the target artery (that cannot be cannulated). A long stent is utilized (usually 38mm). A balloon is then placed over the wire and the stent is mounted on the balloon such that the proximal portion of the stent extends beyond the tip of the balloon on the wire. One or more sutures are used to tie the proximal end of the stent (proximal to the balloon) which will prevent it from expanding (forming a blind-end over the wire, the wire hole will likely occlude). The balloon stent combination is advanced through a sheath into the fenestration such that the tied tip of the stentgraft is distal to the fenestration, and the portion mounted to the balloon is within the fenestration. The balloon is then inflated locking the stentgraft within the fenestration, leaving the blind end distal to the fenestration. The in-fenestration portion of the occluding stentgraft may then be flared as needed.

In certain situations, such as extensive aortic aneurysms, it is necessary to stage procedures with placement of a portion of the stent graft system in one surgical setting and placement of another component in a planned second stage. Many of these first stage procedures are performed with commercially available devices. It is intended that the patient will be considered “enrolled” in this current evaluation when the first non-commercially available device is attempted to be inserted [S263]. In order to better capture the outcomes of overall complex aneurysm repair, the subjects who are treated only with commercially available devices in their first stage of repair will be a part of a parallel registry until the investigational device is implanted at the second stage of repair.

For this registry[S315]:
- Subjects will be consented prior to the first stage of their procedure
- The data for the first stage will be captured in a separate database and will be collected from the subjects medical records
- Subjects will be followed after the first stage as per routine standard of care prior to the fenestrated/branched endograft placement
- Subsequent follow-up intervals will be based on the date of the procedure when the investigational device is implanted

- Reports will include information on all patients enrolled in the study, regardless of whether they have had the investigational device implanted; however, reports for patients that have not had the investigational device implanted will be relatively limited until they receive the investigational device as compliance with the IDE follow-up protocol is not required until after the investigational device is implanted.

Perioperative Care

The endovascular method calls for no departure from the usual perioperative management of patients undergoing aneurysm repair. The preoperative evaluation and intraoperative monitoring will be performed as though the patient was undergoing conventional repair or commercial endovascular repair appropriate to the status of the patient and their co-morbidities. Post-operative management will be dictated by clinical circumstances, and is likely to differ somewhat from the usual management of patients following aneurysm repair, because the patients tend to experience fewer physiologic derangements.

c) Risk Analysis

There are several areas of risk which may be categorized as follows; device complications, adverse events and endoleaks.

i) Device Complications

1) Delivery Issues

- Failure to traverse the iliac arteries
- Improper alignment of stentgraft
- Failure to deploy the stentgraft
- Difficulty with delivery system removal
- Failure to access target vessel (this may or may not be related to device)

2) Graft Integrity Issues

- Migration
- Stent fracture Suture breakage identified as a type III endoleak
- Graft material degradation
- Early Graft infection (occurring within 1 year from the procedure)
- Component separation

ii) Anticipated Adverse Events

There are several categories of anticipated adverse events; cardiovascular, pulmonary, renal, bowel, wound, neurologic and vascular.

The involvement of visceral vessels within the confines of the endograft places these vessels in jeopardy should there be any migration or other stentgraft complications. One considerable risk includes early or late occlusion of the involved visceral vessel. Dissection of the distal aspect of the vessel is possible during the initial implantation of the stent, and may predispose to occlusion. Other causes of visceral vessel occlusion may include mal-alignment of the aortic component, severe angulation within the visceral segment, a size mismatch between visceral vessel and the mating device used, progression of atherosclerotic disease or the development of neointimal hyperplasia.

Pre-existing conditions at admission are not considered adverse events for the purpose of the study analysis (e.g. home oxygen therapy prior to admission). Additionally, common standard of care practices are excluded as adverse events.

Anticipated Adverse Events:

Cardiovascular:

- Myocardial Infarction
- Congestive Heart Failure
- Arrhythmias which require new medication or treatment
- Cardiac ischemia requiring intervention
- Medically intractable hypertension (excludes patients with these conditions pre-procedure)

Pulmonary:

- Respiratory insufficiency/failure (excludes patients with these conditions pre-procedure)
- Pneumonia requiring antibiotics
- COPD (excludes patients with these conditions pre-procedure) exacerbation
- Anaphylactic reaction
- Sepsis
- Post implant syndrome – including fever, leukocytosis, back pain, anorexia and fatigue

Renal:

- Creatinine rise > 30% from baseline on two or more follow-up tests.

This includes creatinine rise caused by renal infarct, renal ischemia or renal occlusion. Creatinine levels will be assessed at 24–48 hours post-procedure or at discharge whichever occurs first. If the first assessment is elevated, confirmatory test will be administered. Both tests must show an elevated (outside the normal range) creatinine level in order to be considered an adverse event. Transient creatinine elevations due to contrast loading or other factors without clinical consequence (normal renal function) are not expected to result in sustained creatinine elevations and therefore, are not considered adverse clinical events for the purpose of this study. Clinically significant renal injury, whether due to contrast, renal artery occlusion, renal perfusion defects, device manipulation or other procedure related causes are intended to be included.

- New renal artery stenosis
- New renal artery occlusions (unintended)
- Renal artery dissections

Bowel:

- Perioperative bowel obstruction
- Bowel Ischemia resulting from the device or procedure
- Aorto-enteric fistula
- Paralytic ileus > 4days (excludes patients with these conditions pre-procedure)

Wound:

- Infection requiring antibiotic treatment
- Hernia
- Lymph fistula
- Dehiscence
- Necrosis requiring debridement (excludes patients with these conditions pre-procedure)
- Hematoma

Neurologic:

- Stroke (thrombotic or hemorrhagic).
- TIA
- Spinal cord ischemia/paralysis (excludes patients with these conditions pre-procedure)
- Paraparesis

Vascular:

- Limb thrombosis
- Venous thrombosis
- Distal embolization resulting in tissue loss or requiring intervention.
- Claudication (excludes patients with these conditions pre-procedure)
- Pseudo-aneurysm
- Acute visceral vessel occlusion

Misplacement of the visceral segment of the endovascular graft will result in malalignment of some or all of the visceral vessels. If this precludes adequate end organ perfusion, then attempts should be made to re-establish flow through the target artery. Considerations will include additional endovascular techniques, extra-anatomic bypass procedures or open surgical conversion. These must be tailored to the patient specific comorbidities.

- Chronic visceral vessel occlusion

Should graft migration occur, stenting of the fenestrated vessel prove impossible, or late vessel thrombosis occur as a result of distal disease, progressive atherosclerosis, restenosis, or simply an acute thromboembolic event, it is possible that a visceral vessel will become occluded remote from the acute endograft implantation time. Although the event may happen and present acutely, it will be consider a chronic visceral vessel occlusion if it occurs > 30 days from the index endograft implantation.

- Visceral vessel dissection

Dissections detected either acutely or chronically will be treated in the presence of flow limiting lesions primarily using distal stenting techniques. If these prove impossible, the involved visceral vessels will be either observed or treated operatively with a distal bypass approach.

- Other vascular injury (other procedure related causes)
- Aneurysm leak or rupture
- Increase in aneurysm size by more than 0.5 cm relative to smallest of any prior measurement
- Coagulopathy
- Impotence

Pain:

- Groin
- Abdominal
- Back

- Extremity (not defined as claudication)

Hemtologic:

- Hemorrhage
- Hypercoagulation
- Anemia
- Sepsis
- DIC
- Need for transfusions

Genitourinary (GU):

- Infection (UTI, bladder, kidney)
- Urethral trauma (unable to void, hematuria, etc.)

iii) Endoleaks

- Type I
- Type II
- Type III
- Type IV
- Type Unknown

iv) Protection Against Risks

Previous clinical and animal experience (in compliance with the Good Laboratory Practice regulations) has been used to achieve the following goals:

- Improve the delivery system
- Develop an adequate insertion and deployment technique
- Determine methods to treat complications
- Improve patient selection

It is hoped that, guided by experience, the above directions will make the endovascular treatment of aortic aneurysms safer and more effective than open surgical repair. Steadily improving results suggest this to be the case.

Potential benefits to the subjects and alternative treatments

The benefits offered to high risk patients are straight forward, as they have few reasonable alternatives available to them, if any at all. The best method to evaluate these benefits is to compare the potential alternative treatment modalities to that of endovascular repair.

Observation

A patient who is not treated is at risk for aneurysm rupture at an overall rate that depends on the aneurysm's size and the patients' longevity. All patients eligible for inclusion in this study have a high risk of rupture, based primarily on aneurysm size or specific morphology. Once the aneurysm has ruptured, it is usually too late to consider treatment in this patient sub-group as most will die, however some of the newly developed techniques can be employed in the setting of emergent/urgent situations and will be tracked in accordance with their presentations.

Conventional surgery

Conventional repair of abdominal aortic aneurysms is highly effective at preventing aneurysm rupture. However, it is associated with a significant degree of cardiopulmonary complications as a result of a prolonged abdominal operation, significant blood loss and aortic cross clamping. High risk patients are defined as such because they do not have enough cardiopulmonary reserve to withstand traditional therapy. Despite the potential for the development of bowel obstructions, graft infections, occlusions and paraanastomotic aneurysms, the long-term risks of open surgical repair are small. The initial physiologic insults are significant and difficult to quantify. A prospective multi-center review involving 666 aneurysm patients calculated a 15 percent risk of cardiac complications, 8.4 percent risk of pulmonary issues, and 6 percent risk of postoperative renal dysfunction. However, these risks were noted to be both surgeon and institution dependent. We presume the complications to be more significant for aneurysms involving or in close proximity to the visceral vessels.

Endovascular repair

In theory, endovascular repair minimizes the physiologic stress of surgery by avoiding aortic cross clamping and celiotomy. There is now an increasing body of data to support that assumption. The reported lower incidence of cardiopulmonary complications noted with endovascular repairs has the potential to significantly benefit patient care. There is significant evidence to support the assumption that aneurysms considered to be excluded based upon CT, angiographic, or ultrasound criteria, have a low risk of rupture. However, aneurysm rupture following endovascular repair can

occur, but generally this is only in the setting of sac reperfusion as a result of device migration, the development of an endoleak, or a device integrity problem resulting in sac repressurization. Therefore, a patient without evidence of endoleak can be considered effectively treated, but must be followed for evidence of any of the above factors that may predispose to rupture. The risk of these problems developing is likely more than that of a conventional repair with an infrarenal device, simply due to the greater number of components. However, the ability to treat to healthy aorta and incorporate branches should provide greater proximal and distal stability of the device.

v) Deaths

Details of any deaths occurring during the evaluation will be collected. Data points include but not limited to:

- Immediate cause of death
- Underlying cause of the fatal condition
- Related to the prosthesis
- Related to the procedure
- Related to a previous condition
- Status of the prosthesis at the time of death

vi) Explants

An autopsy will be requested in all patients who die with an IDE device in place. At the autopsy, the entire abdominal aorta will be excised – from the celiac axis down to and including both common iliac arteries. The specimen will undergo histologic examination.

When the prosthesis is excised in the course of conversion to open repair, the position, and attachment of the prosthesis within the arterial tree will be recorded. In addition, every care will be taken to ensure that the prosthesis is removed intact. For example, vascular clamps will be applied at remote sites from stent attachments. The prosthesis will then be washed with saline to remove surface thrombus. The graft components will be fixed in 4% formaldehyde for subsequent histologic examination. Data will be collected and stored in a database. Data points include but not limited to:

- Date of explant
- Subject's status at explant
- Reason for explant
- Degree of attachment / ingrowth

vii) Loss to Follow-up

If a patient is lost to follow-up, the following information will be recorded:

- Date of last contact with patient
- Reasons for patient's unavailability: withdrawal, moved away, unreachable, and so forth
- Summary of attempts to contact patient
- Name and address of any physician who is following the patient

viii) Study Population

Characteristics

The study population shall consist of female and male subjects, of at least 18 years of age, with aneurysmal disease of the aorta. There is no maximum age; however, patients must have an approximated life expectancy greater than 2 years (except in the setting of emergent or urgent repairs). Racial and ethnic origin is not an issue in this study. In addition, subjects enrolled shall be high risk candidates for open surgical repair and have anatomies unsuitable for currently marketed endovascular stent-grafts.

Prior to enrollment, all subjects shall undergo a general medical evaluation to assess co-morbidities and risk factors associated with aneurysmal disease. All subjects shall undergo preoperative imaging evaluation.

Number of Subjects

Up to 1440 [S323]subjects shall participate in the study. Subject enrollment shall occur on a rolling basis.

d) Device Description

Complete device descriptions are available in Appendix D. In general, devices included in this study include:

1. Custom designed implants constructed with fenestrations and/or side-branches.
2. p-Branch device [S207]
3. Low-Profile custom designed implants constructed with fenestrations and/or side-branches [S306]
4. Hypogastric branch components which include standard helical hypogastric branched device abnd the Bifurcated-Bifurcated hypogastric branched device [S145]

The devices utilized in the study are considered custom implants with the exception of standard p-Branch devices [S207] and hypogastric components [S34, S145]. The stents are made with T-304 stainless steel and nitinol and there are no likely biocompatibility issues related to the stent. The directional branch device [S37,] hypogastric branch device and p-Branch devices are made with combination of both stainless steel and nitinol with no likely biocompatibility issues. The graft material is twill woven from Micrel polyester yarn or Polyethylene terephthalate [PET] fabric. The Low-Profile (LP) devices are constructed with nitinol stents and the same polyester yarn as the standard configuration, but it is more densely and tightly woven [S306]. Biocompatibility issues are unlikely.

Vessels that will be incorporated into the repair will be addressed with the use of a variety of methods including fenestrations and side-arm branches.Descriptions of the device attributes are as follows:

1) Fenestrations: These are circular, elliptical, or hemi-oval openings in the graft fabric. These are intended to be aligned with the target vessel. The fenestration and the target artery are mated with a balloon expandable stent or stentgraft to maintain patency of the vessel and to prevent an endoleak (when mating stentgrafts are utilized). In some cases large fenestrations or hemi-ovals are aligned with the target arteries, but do not require additional stenting to maintain vessel patency.

    a. Initially fenestrations were simply cut into the fabric and mated with the desired stent to adjoin the aortic component with the target vessel.

    b. The addition of a support ring around the fenestrations was employed to improve the sealing between the mating stentgraft and aortic device, as well as to control the intentional fabric defect over time. These are termed reinforced fenestrations [S37]. Fenestrations are termed “small fenestrations” or “large fenestrations.” Small fenestrations are 6-8 mm in height and 6 mm in width, while large fenestrations by be up to 12 mm in height and 12 mm in width [S239]. Fenestrations may be constructed to be strut free. Mulitple fenestrations are permissible on a supporting aortic stent graft to accommodate any number of visceral vessels [S306]. Radiopaque markers are used to outline the edges of the fenestrations.

    c. Modifications of the fenestrations were made over time to provide a means to cannulate the target vessels when exact alignment is not possible or in an effort to avoid customization delays. These fenestrations involve the use of a cone-shaped section of fabric around the fenestration providing a range for the target vessel equal to or in excess of the cone. These fenestrations are termed pivot fenestrations (p-Branch fenestrations or p-Branch devices) [S207]. As with standard fenestrations, radiopaque markers are used to outline the edges of the fenestrations.

2) Side-arm branches: These are extensions of the graft from the main body of the device that are mated with a balloon-expandable or self-expanding stentgraft joining the aortic component and target artery. The overlap segments of such branches may be external, internal or both with respect to the aortic component and will be from 6-8 mm in diameter [S37, S306]. Side-arm branches may be of helical shape or straight [S306]. Side-arm branches may be unsupported or supported with additional nitinol rings.

3) Devices may involve only fenestrations, only side-arm branches or a hybrid construct involving both methods of target branch incorporation. Approved configurations include multiple fenestrations; one directional branch and multiple fenestrations; two directional branches and multiple fenestrations; three directional branches and multiple fenestrations; or four directional branches with no fenestrations [S306].

4) Bridging Stents: Fenestrations and directional branches are mated with their target vessels using a variety of balloon expandable covered stents and/or self-expanding covered stents. The approved bridging stents for specific device constructions are as follows:

a. Reinforced Fenestrations [S37, S55, S272, S284, S295]:

Jomed (Jomed International, Helsingborg, Sweden) stent-grafts	
Stent Diameter	Stent Lengths
4-9 mm	17, 28, 38 mm
6-12 mm	17, 28, 38 mm

iCast Stent Grafts (Atrium Medical Corporation, Hudson, NH)	
Stent Diameter	Stent Lengths
5 mm	16, 22, 38 mm
6 mm	16, 22, 38 mm
7 mm	16, 22, 38 mm
8 mm	38 mm
9 mm	38 mm

CCF Balloon Expandable COVERED STENT (Atrium Medical Corporation, Hudson, NH)	
Stent Diameter	Stent Lengths
5 mm	32 mm
6 mm	32 mm
7 mm	32 mm
8 mm	32 mm

9 mm	32 mm

b. Side-arm branches (Hypogastric and Visceral/Renal): Side-arm branches designed to incorporate the hypogastric, visceral or renal arteries will utilize the following bridging stents:

i. For 6 mm diameter directional branches:

1. 7 or 8 mm Viabahn (Gore Medical, Flagstaff, AZ) stent graft [S34]

2. 8 mm Fluencey stent graft (Bard Medical, Covington, GA) [S39]

3. 7 mm Jomed stent graft [S34] (must have ringed branch)

4. 8 mm iCast stent graft [S34, S55] (must have ringed branch)

ii. For 8 mm diameter directional branches

1. 9 or 10 mm Viabahn (Gore Medical) stent graft [S34]

2. 10 mm Fluencey stent graft (Bard Medical) [S39]

3. 9 mm Jomed stent graft [S34] (must have ringed branch)

4. 10 mm iCast stent graft [S34, S55] (must have ringed branch)

Often a number of commercially available devices are used in conjunction with the investigational devices to ensure the optimal result. Examples include (but not limited to) the following [S148]:

1) Surgical grafts used as conduits or to replace damaged femoral or axillary vessels

2) Self-expanding or balloon expandable stents (examples include SMART stents, Zilver stents, Palmaz stents, Genesis stents, iCast stents, Viabahns, Fluency and others).

3) Occluding devices such as coils or plugs

4) Ancillary devices (examples include Cook TX2P/TX2D, Proform, Renu, Alpha[s316])and so forth

In addition, when the use of the Low-Profile system is utilized for construction of the fenestrated/branched aortic device, the additional use of the Zenith TX2 Low Profile endovascular components may be utilized in order to provide a proximal or distal extension of the Low Profile fenestrated/branched component [S306].

e) Monitoring

Clinical Research Personnel to perform internal QA. IMARC Inc., in conjunction with Cook Research, Inc, will assist with the monitoring of study records for adherence to the study protocol, adequacy of reporting, continued adequacy of facility and staff, and compliance with FDA requirements.

HVI (Heart and Vascular Institute) Research
Cleveland Clinic Foundation
9500 Euclid Ave.
Cleveland, OH 44195

IMARC, Inc.
22560 Lunn Road
Strongsville, OH 44149

Cook Research Inc.
1 Geddes Way
West Lafayette, IN 47906

3)Manufacturing Information

The graft material for the device is manufactured and assembled by Cook, Inc. The device will be constructed, sterilized and loaded into the delivery system by Cook Medical, Inc, Cook Australia, or Cook Europe. The devices will be supplied to the investigators in the same manner (with respect to sterilization and packaging) as the remainder of the investigational devices in the IDE.

Device Manufacturer:

Cook Incorporated P O Box 489 Bloomington, IN 47402-0489 1-800-346-2686	Cook Australia 95 Brandl Street Eight Mile Plains Queensland 4113 Australia 617 384 111 88	William Cook Europe Sandet 6 DK 4632 Bjaeverskov Denmark 45 56 868686

4)Investigator Information

The study shall be conducted at the Cleveland Clinic Foundation by the following investigators:

Matthew Eagleton, MD – Sponsor[S300, S326]/~~Principal Investigator~~[S276 R109]
Federico Parodi, MD [S297] – Principal Investigator [R109]
Behzad Farivar, MD [R109]

Roy K. Greenberg, MD – Sponsor/Principal Investigator (Historical) [S300]
Tara Mastracci, MD – Co-Investigator (Historical) [R038]
Daniel Clair, MD – Co-Investigator (Historical) [R076]
Sean Lyden, MD – Co-Investigator (Historical) [S324]
Eric Roselli, MD – Co-Investigator (Historical) [S324]
Sunita Srivastava, MD – Co-Investigator (Historical) [S324]

All investigators shall agree to conduct the investigation in accordance with the investigational plan, FDA regulations, and IRB guidelines and shall supervise all use of the investigational device involving human subjects and ensure that the requirements for obtaining informed consent is met.

5)IRB Information

The protocol shall be evaluated and approved by the Institutional Review Board at the Cleveland Clinic Foundation prior to proceeding with the study.

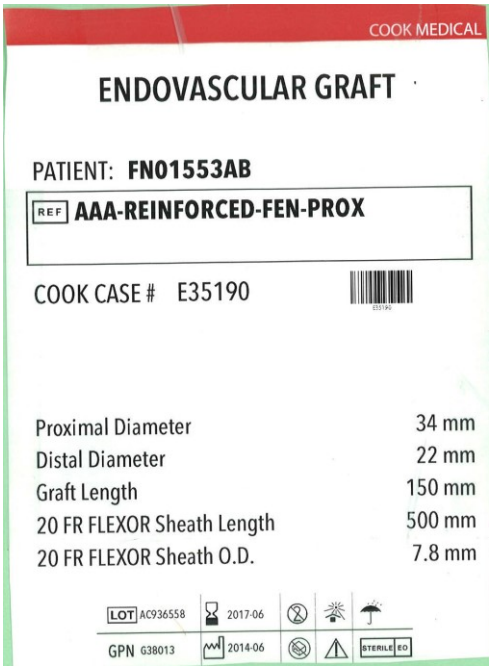
Institutional Review Board
Alan Lichtin, MD – IRB Chairman
Cleveland Clinic Foundation
9500 Euclid Avenue, OS 1
Cleveland, OH 44195
(216) 444-5848

6)Sales Information

The device cost will approximately cover materials and labor for manufacturing. The endovascular stent graft devices used as part of their medical care is billed to the subject and or his medical insurance [S163].

7)Labeling

Sample Label:



8)Subject Recruitment & Informed Consent

Patients referred for abdominal aortic aneurysm, thoracoabdominal aortic aneurysm, iliac aneurysm, renal artery aneurysm or SMA aneurysm repair will be assessed for acceptability into the study. If they meet the clinical and anatomic criteria, the possibility of an endovascular repair will be discussed in the setting of a scheduled office visit.

The investigator will review the patient's history, physical examination, and radiographic studies prior to obtaining informed consent. A written informed consent form will be obtained from the subject after the purposes of the study, the risks, expected discomforts, and potential benefits have been explained. In case of urgent repair utilizing the standard p-Branch devices, the informed consent form may be signed by the subject (if able) or by a family member[S207]. Patients who speak English poorly will have the opportunity to discuss the procedure with the investigator through a translator. The lack of an appropriate translator will be regarded as a barrier to informed consent, thus resulting in exclusion from the study. Copies of the informed consent will be included in the study records. Another copy will be given to the patient.

9) Environmental Impact

Devices shipped under the Investigational Device Exemption are intended to be used for clinical studies in which waste will be controlled or the amount of waste expected to enter the environment may reasonably be expected to be nontoxic.

10) Protocol Amendments

(1) Zip Plug addition, 4/9/2001: S1

(2) Optional ABI or Peripheral Pulses at Follow-up, 2/6/2002: S6

(3) Flexor Delivery System, 8/20/2002: S# unknown

(4) Study Expansion- 50 additional patients, 2/20/2003: S13

(5) Optional Purse String Tie, 5/29/2003: S# unknown

(6) New CRFs and Introduction of Oracle Database, 12/2/2003: S# unknown

(7) Hypogastric Branch Device Addendum, 4/19/2004: S34

(8) Branch Technology, new CRFs, new devices, 7/6/2004: S37

(9) Additional Fluency Device, 8/31/2004: S39

(10) New Co-Investigator, new CRFs, 9/21/2004: S40

(11) Modification of inclusion criteria to treat renal artery aneurysm, 3/9/2005: S45

(12) Addition of iCast Device, 9/29/2005: S63

(13) New Co-Investigators (Matthew Eagleton, Eric Roselli), 3/13/2006:S# unknown

(14) Study Expansion- 50 additional patients, 3/21/2006: S74

(15) New Co-Investigator (Sunita Srivastava) 4/3/2006: S# unknown

(16) Superflex delivery system to be used on TAA devices, 8/1/2006: S# unknown

(17) Addition of Polyurethane Vessel Dilators, 8/28/2006: S# unknown

(18) Optional Discharge Datapoints, 8/29/2006: S# unknown

(19) Study Expansion- 50 additional patients, 11/21/2006: S98

(20) Study Expansion- 50 additional patients, 7/17/2007: S114

(21) Study Expansion- 100 additional patients, 4/8/2008: S127

(22) Optional 6 month visit, 5/1/2008: S128

(23) New Co-Investigator (Tara Mastracci), 7/9/2008: S129

(24) Change of address for one manufacturing plant (Cook Australia), 9/22/2008: S133

(25) Study Expansion – 100 additional patients, 2/26/2009: S141

(26) Update in monitoring plan, 2/26/2009: S140

(27) Bifurcated-bifurcated (Bif-bif) Device Addendum, 3/20/2009: S145

(28) Cleveland Clinic Vascular Surgery Change of Address, 5/4/2009: S147

(29) Clarification of Use of Off-the-shelf Devices, 5/8/2009: S148

(30) Addition of Modified Iliac (Flexor) Component, 9/30/2009: S162

(31) Addition of ZHIS Curved Catheter, 11/16/2009: S164

(32) Study Expansion – 100 additional patients, 2/10/2010: S175

(33) Addition of Proform, 3/22/2010: S178

(34) Clarification of Trigger Wires, 3/29/2010: S179

(35) Change in Ultrasound Schedule, 8/12/2010: S187

(36) Addition of Preloaded Device, 9/13/2010: S189, S201

(37) Study Expansion – 20 additional patients, 11/3/2010: S195

(38) Addition of Spiral Trigger Wire, 11/5/2010: S194

(39) Change in IDE Title, 12/3/2010: S203

(40) Addition of p-Branch Device, 2/15/2011: S207

(41) Study Expansion – 100 additional subjects, 4/12/2011: S216

(42) Modified Hypogastric Branch Device, 5/18/2011: S219

(43) Addition of Spiral-Z Device, 7/22/2011: S226

(44) Revised General Inclusion Criteria, 9/1/2011: S229

(45) Modified Anatomic Inclusion Criteria for Hypogastric Branch Device, 9/29/2011: S232

(46) Modified Inclusion Criteria for Urgent p-Branch cases, 11/2/2011: S235

(47) Clarification of Anatomic Inclusion Criteria re: landing zones, 1/12/2012: S238

(48) Clarification of large fenestration, 1/11/2012: S239

(49) Clarification of optional datapoint re: date of resumption of ambulation, 1/11/2012: S240

(50) Study Expansion – 130 additional subjects. 3/29/2012: S245

(51) Dr. Eagleton as Study P. I., 2/25/2013: S276

(52) Study Expansion – 100 additional subjects, 5/30/2013: S286

(53) Addition of Dr. Parodi as a Co-Investigator, 11/26/2013: S297

(54) Transfer of Sponsorship to Dr. Eagleton, 1/24/2014: S300

(55) Removing Dr. Mastracci, 7/29/2014: R038

(56) Database Transfer from Oracle Clinical to OmniComm, 9/29/2014: R042

(57) p-Branch distal diameter change to 22 mm: 10/13/2014, S304

(58) Updated IOP re: Reportable Events: 11/6/2014, S305

(59) Preloaded-Preloaded LP device addendum: 11/11/2014, S306

(60) p-Branch construction changes: 1/5/2015, S307

(61) Study Expansion: 1/1/2015, S308

(62) Study Expansion: 3/9/2015, S309

(63) Master Protocol reflecting the change approved in S309: 4/13/2015, S311

(64) Clarification of Study Enrollment – Additional Information for S311: 6/5/2015, S312

(65) Clarification of Study Enrollment and Staged Procedure Registry: 8/10/2015, S313

(66) Clarification of S313, Master Protocol Modification: 11/2/2015, S315

(67) Addition of Cook Alpha Device: 1/28/2016, S316

(68) Removing Dr. Clair: 2/23/2016, R076

(69) Study Expansion (additional 120 subjects, total 1340): 3/7/2016, S318

(70) Clarification of Proximal Neck Length for Juxtarenal Aneurysm Repair, S# 322

(71) Study Expansion (additional 100 Subjects, total 1440): 5/1/2017, S323

(72) Removing Drs. Lyden, Roselli and Srivastava from the study: 6/6/2017, S324

(73) Dr. Eagleton leaving Cleveland Clinic on 12/15/2017, Dr. Parodi as PI, Dr. Farivar added as Co-investigator: 11/6/2017, S326

(74) Fenestrated Device Group Final Report: 12/12/2017, R109