CLINICAL INVESTIGATION PLAN

Zenith® p-Branch™ Pivotal Study

Global Clinical Number 14-09
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Sponsor: Cook Research Incorporated
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West Lafayette, IN 47906
USA

CLINICAL INVESTIGATION PLAN SIGNATURE PAGE

This clinical investigation will be conducted in compliance with the Clinical Investigation Plan (CIP), ISO 14155, ICH GCP, 21 CFR 812, and other applicable requirements as appropriate.

Signatures:

Sponsor Contact

Signature	DD/MM/YYYY
Printed Name	Title

CLINICAL INVESTIGATION PLAN SIGNATURE PAGE, CONTINUED

National Principal Investigator

I hereby confirm that I approve of this Clinical Investigation Plan (CIP) and agree to comply with its terms as laid out in this document.

Signature	DD/MM/YYYY
Printed Name	Title

CLINICAL INVESTIGATION PLAN SIGNATURE PAGE, CONTINUED

Principal Clinical Investigator

I hereby confirm that I approve of this Clinical Investigation Plan (CIP) and agree to comply with its terms as laid out in this document.

Signature	DD/MM/YYYY
Printed Name	Title

CONFIDENTIALITY STATEMENT

This document shall be treated as a confidential document for the sole information and use of the clinical investigation team and Institutional Review Board (IRB).

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1.0 Clinical Investigation Plan Overview

This clinical investigation is intended to evaluate the safety and effectiveness of the Zenith® p-Branch™ in combination with Atrium iCAST™ covered stents for the treatment of pararenal or juxtarenal aortic aneurysms. The primary safety and effectiveness endpoint is treatment success at 12 months. This prospective, non-randomized, multicenter clinical investigation will enroll 80 patients to receive the Zenith® p-Branch™ at up to 30 clinical sites (maximum of 20 patients per site). Patient enrollment is expected to be completed within 2.5 years of study initiation. Follow-up data will be collected for 5 years post-procedure.

Patients with a pararenal or juxtarenal abdominal aortic aneurysm (AAA) ≥5.0 cm in diameter (or 2 times normal aortic diameter), history of growth ≥0.5 cm/year, or saccular aneurysm with aortic diameter greater than 1.5 times the normal aortic diameter that is deemed to be at risk for rupture based upon physician interpretation, with anatomy suitable for treatment with the Zenith® p-Branch™ may be eligible for enrollment. The study flow diagram is presented in Figure 1.1.

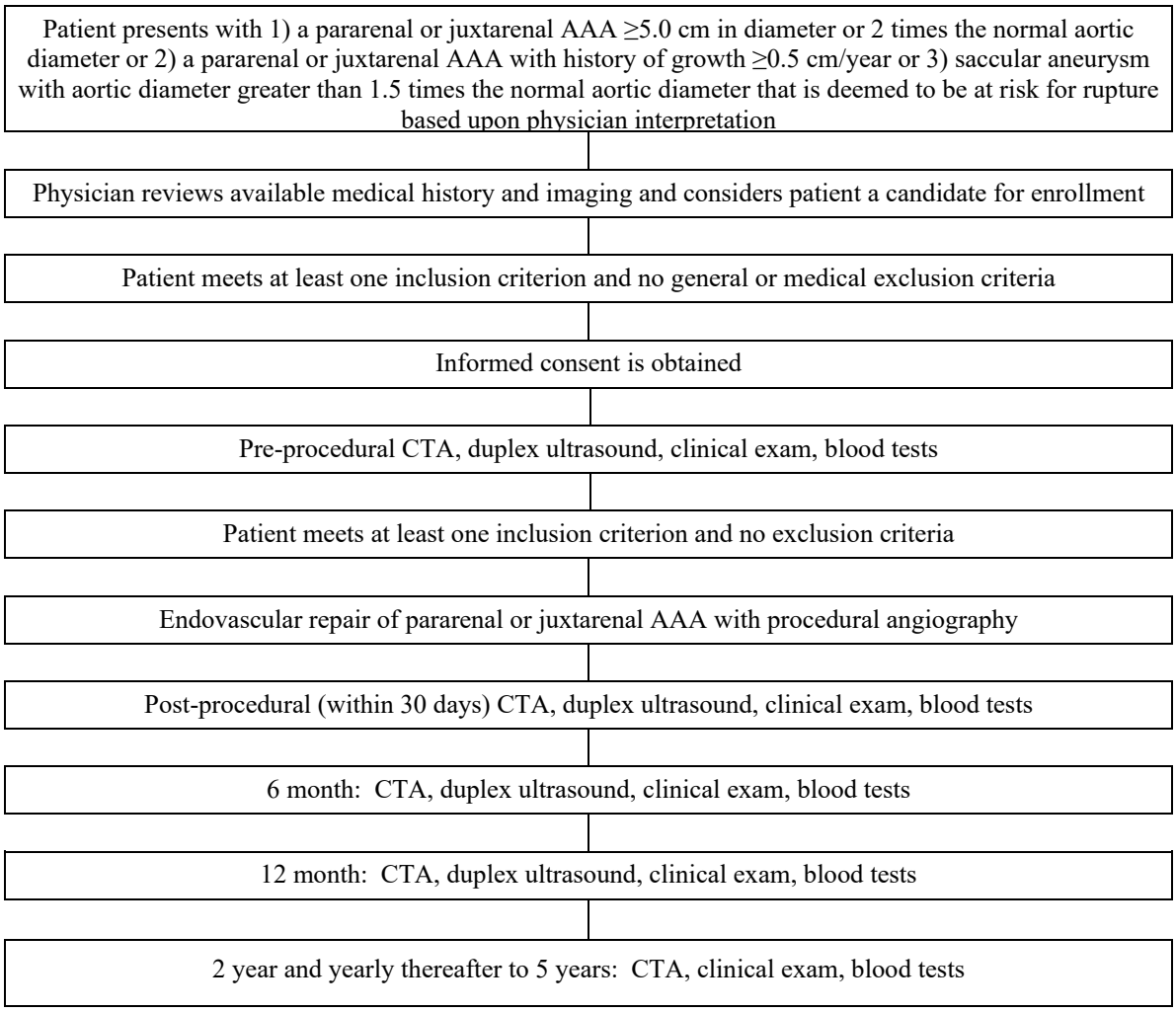

Figure 1.1. Study flow diagram.

2.0 Objectives of the Clinical Investigation

2.1 Primary Objective

The primary objective of this study is to evaluate the safety and effectiveness of the Zenith® p-Branch™ used for treatment of pararenal or juxtarenal AAAs. Safety and effectiveness will be measured by the rate of treatment success at 12 months.

Treatment success is defined as technical success and freedom from all of the following at 12 months:

- Type I or Type III endoleaks that require intervention post-discharge (including Type I and Type III endoleaks identified for treatment on the 12 month follow-up CT);
- Aneurysm growth > 0.5 cm;
- AAA related serious adverse event (i.e. death, rupture, or conversion to open surgical repair);
- AAA-related major complication (i.e. renal failure requiring permanent dialysis, bowel obstruction, ischemia, or fistula, stroke with permanent deficit, or paralysis).

2.2 Secondary Objectives

In addition to the primary objective stated above, the following secondary objectives, evaluated for descriptive purposes (not for the purpose of statistical inference), include an assessment of the following:

- Myocardial infarction (MI)
- Congestive heart failure (CHF)
- Cardiac ischemia requiring intervention
- Visceral vessel events
- Changes in aneurysm size
- Secondary interventions
- Endoleak
- Device migration
- Device patency
- Device integrity

3.0 Device Description and Intended Use

3.1 General Device Description

The Zenith® p-Branch™ is part of a modular system which may include a distal bifurcated device (Zenith® Universal Distal Body Endovascular Graft) and iliac leg devices (Zenith® Spiral-Z® AAA Iliac Leg Graft), as shown in Figure 3.1.

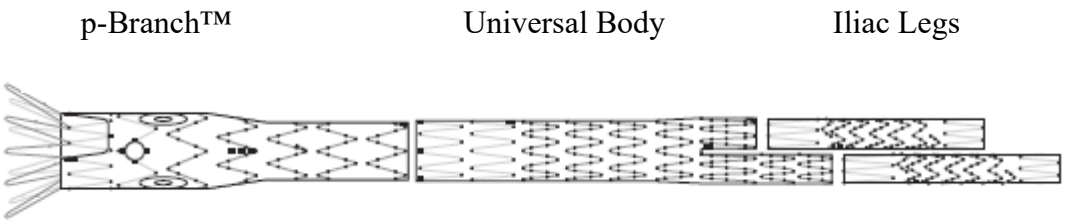

Figure 3.1. Zenith® p-Branch™ is part of a modular system that may include a bifurcated device (Zenith® Universal Distal Body Endovascular Graft) and commercially available Zenith® Spiral-Z® AAA Iliac Leg Grafts.

3.1.1 Zenith® p-Branch™

The Zenith® p-Branch™ is a modular system (Figure 3.1) constructed of full-thickness woven polyester fabric sewn to self-expanding stainless steel and nitinol Z-stents, and is introduced using the Zenith® preloaded delivery system (Figures 3.2 and 3.3). Three fenestrations and a scallop in the graft material preserve blood flow to the renal and visceral vessels. The two renal artery fenestrations are conical-shaped and may be manipulated to accommodate a range of renal anatomies with a single design. The endovascular graft is available in two fenestration/scallop configurations (A and B) to provide an optimal fit for individual patient anatomies (Figures 3.4 and 3.5). Refer to the Manufacturer's Instructions for Use (IFU) for the device sizes available and planning and sizing information for the clinical investigation.

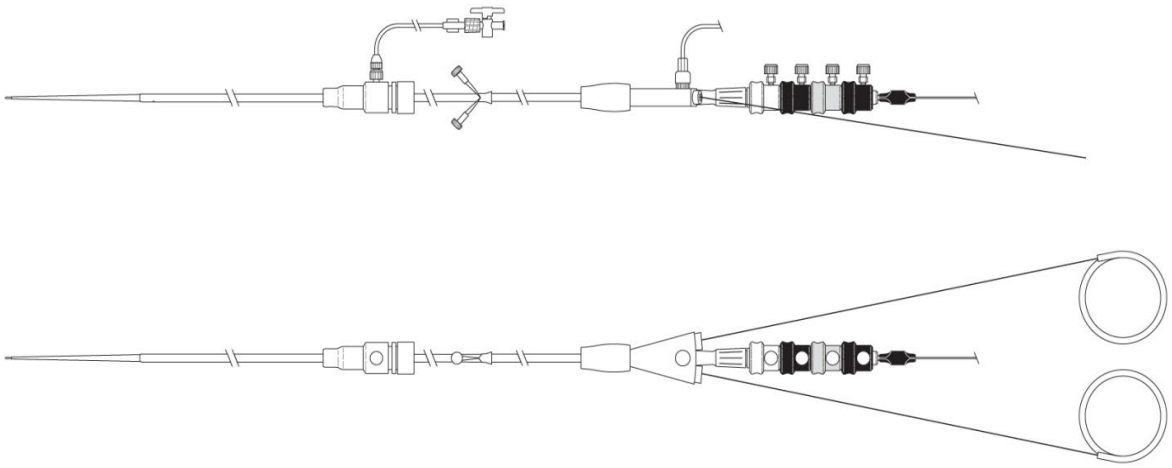

Figure 3.2. Zenith® preloaded delivery system showing preloaded nitinol wire.

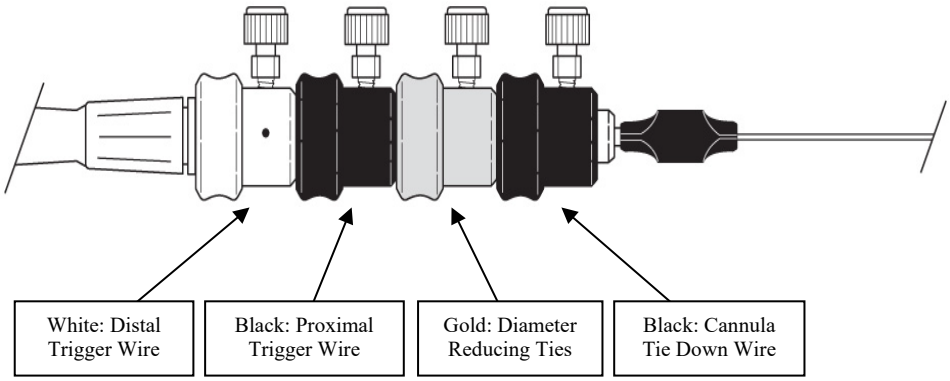

Figure 3.3. Detail of the release handles of the Zenith® preloaded delivery system.

Configuration A:

- Celiac scallop: 20 mm wide, centered at 12:30 o'clock (15°) 11 mm above SMA;
- SMA fenestration: 8 mm diameter, located at 12:00 o'clock (0°);
- Right pivot (renal) fenestration: 6 mm inner and 15 mm outer diameter, 5 mm deep, oriented at 9:30 o'clock (285°), 12 mm below SMA (center-to-center);
- Left pivot (renal) fenestration: 6 mm inner and 15 mm outer diameter, 5 mm deep, oriented at 2:30 o'clock (75°), 12 mm below SMA (center-to-center).

Configuration B:

- Celiac scallop: 30 mm wide, centered at 12:30 o'clock (15°), 9 mm above SMA;
- SMA fenestration: 8 mm diameter, located at 12:00 o'clock (0°);
- Right pivot (renal) fenestration: 6 mm inner and 15 mm outer diameter, 5 mm deep, oriented at 9:30 o'clock (285°), 16 mm below SMA (center-to-center);
- Left pivot (renal) fenestration: 6 mm inner and 15 mm outer diameter, 5 mm deep, oriented at 2:30 o'clock (75°), 20 mm below SMA (center-to-center).

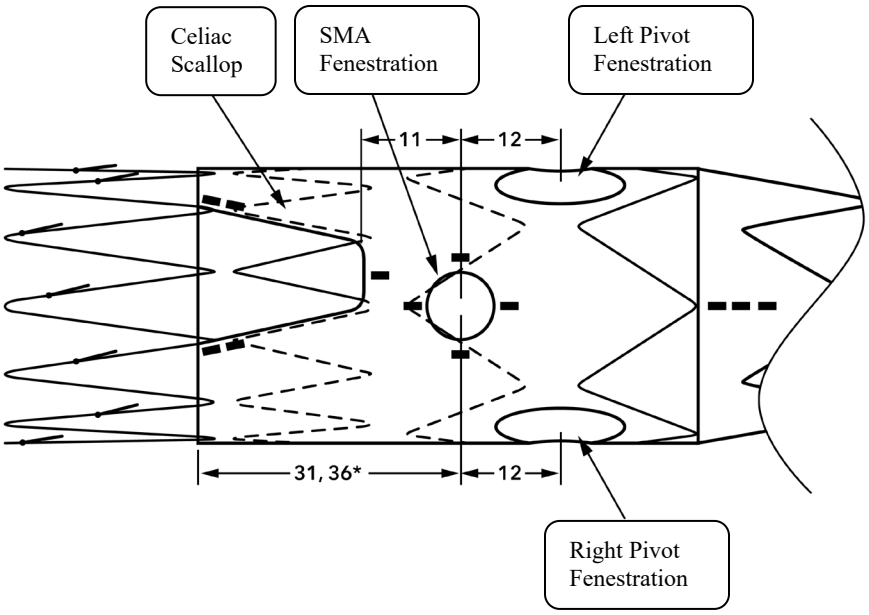

Figure 3.4. Configuration A fenestration locations.
*For 36 mm diameter grafts only

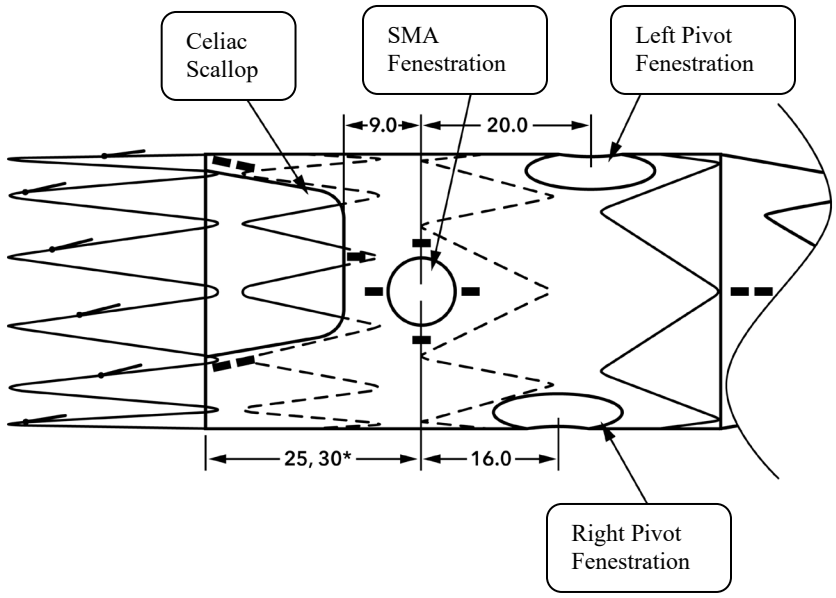

Figure 3.5. Configuration B fenestration locations.
*For 36 mm diameter grafts only

Anatomical Criteria

Zenith® p-Branch™ endovascular graft configuration A or B will be chosen in accordance with the following criteria. All radial measurements are calculated assuming the SMA position is 12:00 o'clock (0°). Refer to the Investigator's Brochure for more details about the anatomical criteria.

1. Criteria for configuration A (renal fenestrations at same longitudinal level):
    a. The celiac artery arises from the aorta between 11:30 o'clock and 1:30 o'clock (345° and 45°) or arises above the top of the graft;
    b. The SMA is ≥11 mm distal to the celiac artery (unless the celiac artery is occluded or expendable);
    c. Longitudinal positions of renal arteries arise 4.5 mm – 19.5 mm distal to the SMA;
    d. The circumferential location of the right renal artery can range between 8:30 o'clock and 10:30 o'clock (255° and 315°) and the circumferential location of the left renal artery can range between 1:30 o'clock and 3:30 o'clock (45° and 105°) (assuming the endovascular graft diameter is approximately 30 mm).
2. Criteria for configuration B (left renal fenestration lower longitudinally than right renal fenestration):
    a. The celiac artery arises from the aorta between 11:00 o'clock and 2:00 o'clock (330° and 60°) or arises above the top of the graft;
    b. The SMA is ≥9 mm distal to the celiac artery (unless the celiac artery is occluded or expendable);
    c. Longitudinal position of the right renal artery arises 8.5 mm – 23.5 mm distal to the SMA;
    d. Longitudinal position of the left renal artery arises 12.5 mm – 27.5 mm distal to the SMA;
    e. The circumferential location of the right renal artery can range between 8:30 o'clock and 10:30 o'clock (255° and 315°) and the circumferential location of the left renal artery can range between 1:30 o'clock and 3:30 o'clock (45° and 105°) (assuming the endovascular graft diameter is approximately 30 mm).

3.1.2 Zenith® Universal Distal Body Endovascular Graft

The Zenith® p-Branch™ is designed to be used with the Zenith® Universal Distal Body Endovascular Graft (Figure 3.6). The Zenith® Universal Distal Body Endovascular Graft is delivered with the H&L-B

One-Shot™ Introduction System (Figure 3.7). Refer to the Manufacturer's Instructions for Use (IFU) for the device sizes available and sizing information.

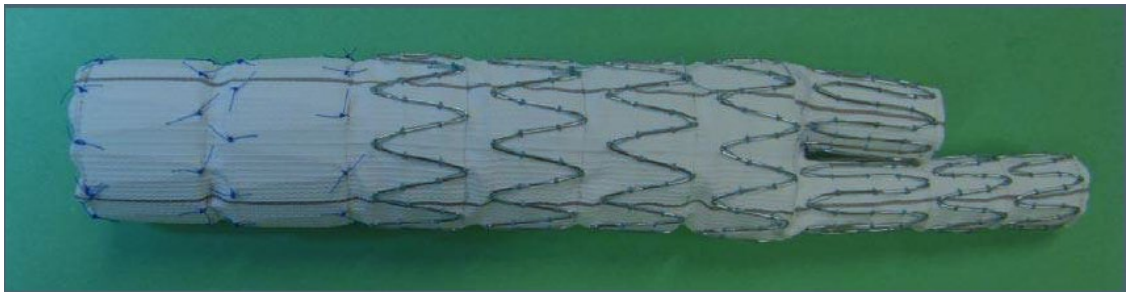

Figure 3.6. Zenith® Universal Distal Body Endovascular Graft.

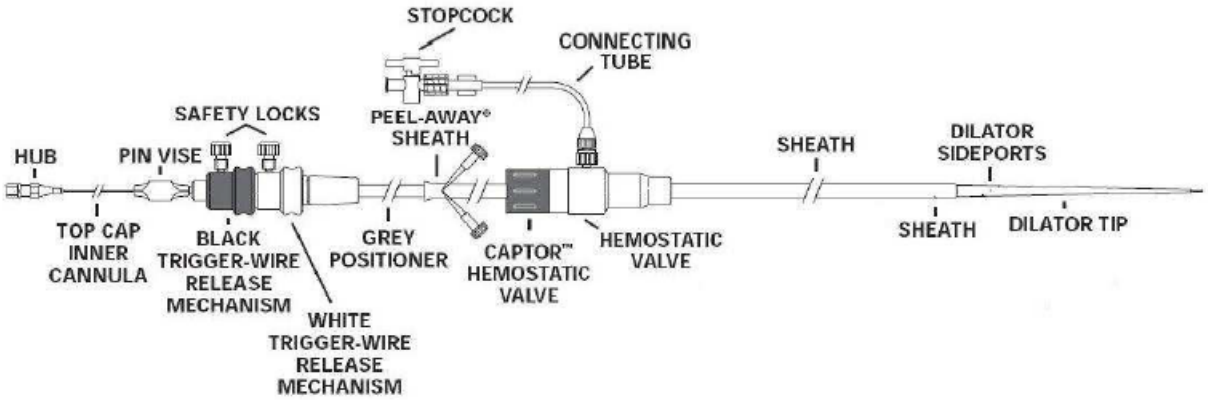

Figure 3.7. H&L-B One-Shot™ Introduction System.

3.1.3. Atrium iCAST™ Stent

Commercially available Atrium iCAST™ stents will be used in conjunction with the Zenith® p-Branch™ to preserve blood flow to the visceral vessels. The Atrium iCAST™ covered stent is a balloon-expandable endoluminal device consisting of a laser cut 316L stainless steel stent with an encapsulated cover made of expanded polytetrafluoroethylene (PTFE). The sizes listed in Table 3.1 reflect the subset of commercially available sizes that are recommended for use in combination with the Zenith® p-Branch™ as part of the study**.**

Table 3.1. Atrium iCAST™ covered stent availability.

Diameter (mm)	Length (mm)	Catheter Length* (cm)	Introducer (Fr)
5	16	80 or 120	6
5	22	80 or 120	6
6	16	80 or 120	6
6	22	80 or 120	6
7	22	80 or 120	7
7	38	80 or 120	7
8	38	80 or 120	7
9	38	80 or 120	7
10	38	80 or 120	7

*Stents intended for placement in renal arteries must use 120 cm catheters and be of a compatible French size to extend through the 90 cm sheaths used with Zenith® p-Branch™.

3.1.4 Other Devices

Other commercially available Zenith® endovascular devices such as main body extensions, iliac leg extensions, converters, and iliac plugs may also be required during an aortic endovascular procedure. Each individual device has its own Instructions for Use.

3.2 Indication for Use

The Zenith® p-Branch™ is indicated for the endovascular treatment of patients with pararenal or juxtarenal AAA having morphology suitable for endovascular repair. Refer to the Manufacturer's Instructions for Use for details regarding indications for use.

3.3 Product Identification and Tracking

The identification and labeling of the products under investigation are outlined in the Investigator's Brochure and Manufacturer's Instructions for Use.

Products under investigation will be tracked throughout the course of the clinical investigation through use of a Product Log, upon which lot numbers, quantity, and disposition of product will be recorded. Product Logs will be maintained in the site's Investigator File. Additionally, the quantity(s), size(s), and lot number(s) of products used in patients will be recorded on case report forms (CRFs).

3.4 Instructions for Use

Refer to the Manufacturer's Instructions for Use for complete instructions including device sizes, installation, storage and handling requirements, preparation for use, and any intended re-use, pre-use checks for safety and performance, and precautions to be taken after use.

3.5 Summary of Necessary Training and Experience

Please reference the Manufacturer's Instructions for Use for a complete summary of the necessary training and experience required for use of this product.

3.6 Description of the Necessary Medical or Surgical Procedures

Refer to the Manufacturer's Instructions for Use for a complete description of the procedures involved in the use of this product.

4.0 Summary of Preliminary Investigations

Refer to the Investigator's Brochure for a summary of non-clinical testing and a summary of previous clinical experiences with the device or other similar devices.

5.0 Risk Analysis and Risk Assessment

Refer to the Investigator's Brochure for a summary of benefits and a complete risk analysis.

5.1 Risks and Foreseeable Adverse Device Effects

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

- 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 and/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 transient or permanent ischemia or infarction;
- Endoleak;
- Endoprosthesis: improper component placement, incomplete component deployment, component migration, suture break, occlusion, infection, stent fracture, graft material wear, dilatation, erosion, puncture, perigraft flow, barb separation, and corrosion;
- Fever and localized inflammation;
- Genitourinary complications and subsequent attendant problems (e.g., ischemia, erosion, fistula, incontinence, hematuria, infection);
- Graft or native vessel occlusion;
- Hepatic failure;
- Impotence;
- Infection of the aneurysm, device, or access site, including abscess formation, transient fever, and pain;
- Lymphatic complications and subsequent attendant problems (e.g., lymph fistula);
- Neurologic local or systemic complications and subsequent attendant problems (e.g., stroke, transient ischemic attack, paraplegia, paraparesis, paralysis);
- Open surgical conversion;
- Pulmonary/respiratory complications and subsequent attendant problems (e.g., pneumonia, respiratory failure, prolonged intubation);
- Renal complications and subsequent attendant problems (e.g., infarction, artery occlusion, contrast toxicity, insufficiency, failure);
- Splenic injury (e.g., infarction, ischemia);
- Vascular access site complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula;
- Vessel damage;

- Wound complications and subsequent attendant problems (e.g., dehiscence, infection);
- Vascular spasm or vascular trauma (e.g., iliofemoral vessel dissection, bleeding, rupture, death).

5.2 Methods to Minimize Risks

This device will be used only by trained healthcare professionals who are experienced in the study procedure. Patients will be selected according to the labeled indication and in accordance with inclusion/exclusion criteria outlined in this document.

The device design, non-clinical testing, clinical study design, and the Manufacturer's Instructions for Use are intended to minimize the risks associated with the use of this device. The risks of the study have been minimized and the potential benefits and the importance of the knowledge to be gained about the safety and effectiveness of the device outweigh the risks.

6.0 Design of the Clinical Investigation

6.1 Type of Investigation

This prospective, non-randomized, multicenter clinical investigation will evaluate the safety and effectiveness of the the Zenith® p-Branch™ in combination with Atrium iCAST™ covered stents for the treatment of pararenal or juxtarenal aortic aneurysms. This study will enroll 80 patients at up to 30 clinical sites. Patient enrollment is expected to be completed within 2.5 years of study initiation. Follow-up data will be collected for 5 years post-procedure. The total study duration should be approximately 7.5 years.

6.2 Inclusion and Exclusion Criteria

Assessment of selection criteria will be based upon data available pre-operatively. Data obtained peri-operatively and post-operatively (including the results from core laboratory analysis of pre-procedure imaging) may contradict pre-operative assessment. However, such contradiction is not considered a violation of the Clinical Investigation Plan and should not be construed as evidence of inadequate or inaccurate pre-operative assessment with respect to the enrollment criteria or evidence of inappropriate enrollment. Enrollment is to be based upon best available pre-operative data. Some criteria relate to subjective assessment while other criteria are considered absolute and are able to be determined

definitively. Variability in assessment between centers, investigators, and observers is expected with several criteria.

6.2.1 Inclusion Criteria

A patient is deemed suitable for inclusion in the study if the patient meets at least one the following criteria:

1. Pararenal or juxtarenal AAA ≥5.0 cm in diameter or 2 times the normal aortic diameter;
2. Pararenal or juxtarenal AAA with history of growth ≥0.5 cm/year;
3. Saccular aneurysm with aortic diameter greater than 1.5 times the normal aortic diameter that is deemed to be at risk for rupture based upon physician interpretation.

6.2.2 Exclusion Criteria

General Exclusion Criteria

A patient must be excluded from the clinical investigation if any of the following are true:

1. Age <18 years;
2. Life expectancy <2 years;
3. Pregnant, breast-feeding, or planning on becoming pregnant within 60 months;
4. Inability or refusal to give informed consent by the patient or a legally authorized representative;
5. Unwilling or unable to comply with the follow-up schedule;
6. Simultaneously participating in another investigative device or drug study. (The patient must have completed the primary endpoint of any previous study at least 30 days prior to enrollment in this study.)

Medical Exclusion Criteria

A patient must be excluded from the clinical investigation if any of the following are true:

1. Leaking, ruptured, or mycotic aneurysm;
2. Active systemic infection (e.g., sepsis);
3. Serum creatinine level >2.0 mg/dl;
4. Patient does not have two viable renal arteries intended to be accommodated by the pivot fenestrations;

5. Significant surgical procedures (including endovascular repair) within 30 days before or after aneurysm repair;
6. Presence of a stent in any vessel to be accommodated with a fenestration that will interfere with deployment of the Zenith® p-Branch™ or stenting of renal and visceral vessels accommodated by a fenestration;
7. Previous endograft in the abdominal aorta;
8. Bleeding, diathesis, or uncorrectable coagulopathy;
9. Refuses blood transfusion;
10. Allergy to materials of the graft(s) or their delivery systems (stainless steel, nitinol, polyester, solder [tin, silver], polypropylene, urethane, or gold) or the Atrium iCAST™ stent (stainless steel or polytetrafluoroethylene);
11. Anaphylactic reaction to contrast that cannot be adequately pre-medicated.

Anatomical Exclusion Criteria

A patient must be excluded from the clinical investigation if any of the following are true:

1. Suitable proximal neck for treatment with a standard Zenith® AAA Endovascular Graft;
2. Infra-SMA sealing zone length < 4 mm;
3. Greater than 10% increase in diameter over the length of the proximal sealing zone;
4. Proximal sealing zone angulated > 60 degrees relative to the centerline of the aneurysm or proximal sealing zone angulated > 45 degrees relative to the supraceliac aorta;
5. Proximal sealing zone diameter > 32 mm or < 21 mm (measurements based on outer diameter unless evidence of vessel thickening);
6. Renal and visceral vessel anatomy incompatible with graft or fenestration stents (see Section 3.1, subsection *Anatomical Criteria*, for more details on the renal and visceral vessel criteria and Section 3.1 for more details on fenestration stents);
7. Non-bifurcated segment of any artery to be stented < 15 mm in length if use of covered stent is planned;
8. Renal artery or SMA stenosis > 50%;
9. Renal artery diameter < 5 mm;
10. SMA diameter < 6 mm or ≥ 12 mm;
11. Sacrifice of IMA, accessory renal arteries, or internal iliac arteries that would significantly compromise physiological function in the opinion of the investigator;

12. Distance from the distal-most aspect of the lowest renal artery to the aortic bifurcation that is incompatible with the available lengths of the Zenith® Universal Distal Body Endovascular Graft (if used);
13. Distance from the center of the SMA to the aortic bifurcation that is incompatible with the available lengths of the Zenith® p-Branch™;
14. Prohibitive occlusive disease, calcification, or thrombus of the proximal sealing zone;
15. Tortuosity, calcification, or arterial diameter not conducive to placement of the introducer with use of a conduit;
16. Unsuitable arterial anatomy.

6.3 Endpoints

6.3.1 Primary Endpoints

The primary safety and effectiveness endpoint is treatment success at 12 months. Treatment success is defined as technical success and freedom from all of the following at 12 months:

- Type I or Type III endoleaks that require intervention post-discharge (including Type I and Type III endoleaks identified for treatment on the 12 month follow-up CT);
- Aneurysm growth > 0.5 cm;
- AAA related serious adverse events (i.e., death, rupture, or conversion to open surgical repair) as adjudicated by an independent CEC;
- AAA-related major complications (i.e., renal failure requiring permanent dialysis; bowel obstruction, ischemia, or fistula; stroke with permanent deficit; or paralysis) as adjudicated by an independent CEC.

6.3.2 Secondary Endpoints

The following secondary endpoints will be evaluated for descriptive purposes (not for the purpose of statistical inference):

- Myocardial infarction
- Congestive heart failure
- Cardiac ischemia requiring intervention
- Visceral vessel events
- Changes in aneurysm size
- Secondary interventions

- Endoleak
- Device migration
- Device patency
- Device integrity

6.3.3 Rationale for Endpoints

The primary endpoint incorporates the measures relevant to fully evaluate the safety and effectiveness of the Zenith® p-Branch™. Specifically, success first requires graft deployment in the intended location with patency of all vessels targeted by a fenestration (i.e., technical success). A patient must be free from Type I endoleak requiring intervention, which is relevant given that the device is intended to provide aneurysm exclusion. Likewise, a patient must be free from Type III endoleak requiring intervention, which is relevant given the use of covered stents in contributing to sealing of the aneurysm at the junction with a fenestration. Not only must patients be free from AAA-related serious adverse events (death rupture, or conversion to open surgical repair), but they must also be free from major complications (stroke with permanent deficit and paralysis) and related events specific to the target vessels (e.g., renal failure requiring dialysis, bowel obstruction, ischemia, or fistula).

6.4 Variables to be Measured to Demonstrate Achievement of Endpoints

The safety and effectiveness endpoint measured by treatment success at 12 months will be assessed by collecting and analyzing the following data:

- Technical success will be determined by collecting deployment information and procedural angiography;
- Type I and III endoleaks will be assessed by CT at each follow-up visit;
- Aneurysm growth >0.5 cm will be assessed by comparing the maximum aneurysm diameter measurement on each follow-up CT (post-procedure CT measurement should be considered baseline);
- SAEs and major complications will be assessed by clinical exams at each follow up.

Independent core laboratories (to be designated) will be used to provide detailed analysis for data collected (e.g., angiographic, ultrasound, CT, X–ray, and MRI).

The clinical data and imaging measurements will be collected on standardized CRFs, which may serve as source documents. The schedule for assessments is summarized in Table 6.1.

Table 6.1. Data collection schedule

	Pre-procedure	Procedure	Post-procedure[1]	6 month	12 month	2 year[2]
CTA[3]	X[4]		X[5]	X[5]	X[5]	X[5]
Angiography		X				
Duplex ultrasound[6]	X		X	X	X	
Clinical exam	X		X	X	X	X
Blood test[7]	X		X	X	X	X

[1] Post-procedure follow-up within 30 days of procedure.
[2] Patients will be followed up at yearly intervals through five years.
[3] Device X-rays may be requested to provide more focused imaging if potential device integrity issues are identified, but are unable to be confirmed, using CT.
[4]Imaging should be performed within 6 months of the procedure, with imaging within 3 months of the procedure considered to be optimum.
[5] Duplex ultrasound and non-contrast CT may be used for those patients experiencing documented renal failure or who are otherwise unable to undergo a contrast-enhanced CTA scan.
[6] In cases of reinterventions for stenosis/occlusion of a branch vessel targeted by a fenestration, duplex ultrasound should be performed prior to the reintervention procedure.
[7] Required blood tests include creatinine, BUN, AST, and ALT.

6.5 Measures to be Taken to Avoid or Minimize Bias

This clinical investigation is not randomized or blinded. It is intended to collect information regarding physician use of the Zenith® p-Branch™. The study will utilize uniform definitions for study endpoints, event adjudication by an independent clinical events committee, and imaging data analysis by a centralized core laboratory. Study results will be analyzed in accordance with a prospectively defined analysis plan.

7.0 Methods

7.1 Patient Assessment, Screening, and Consent

Patients will be screened to ensure they meet the inclusion criteria and do not meet any of the exclusion criteria. Patients who meet the inclusion criteria and do not meet any of the exclusion criteria will be invited to participate in this investigation. All patients eligible for entry into the investigation will have the Clinical Investigation Plan explained to them, as well as the potential risks and benefits of their participation in the investigation. Each patient who agrees to participate, or a legally authorized representative, will be required to sign an informed consent document prior to the procedure. If new

information is obtained after a patient receives treatment with the device, patients who have not exited the study will be informed about the new information, and will be re-consented at the discretion of the investigator and/or the site's IRB.

7.2 Point of Enrollment

Point of enrollment will be based on the intent-to-treat population and is defined to include any patient for whom the treatment procedure is initiated. More specifically, the patient would be included in the intent-to-treat population upon procedure initiation (i.e., cutdown or initiation of percutaneous access). Informed consent will be obtained and assessment of the patient's conformance to the inclusion/exclusion criteria will occur prior to the procedure.

7.3 Medications

The hospital's standard protocol should be followed with respect to medication. Dual anti-platelet therapy is recommended for three months following the index endovascular procedure or after a secondary intervention involving the visceral vessels. Aspirin therapy is recommended indefinitely.

7.4 Pre-procedure

Planning and sizing of the Zenith® p-Branch™ endovascular graft is completed pre-operatively based on radiologic assessments, including CTA.

7.5 Procedure

Each patient will receive one Zenith® p-Branch™ endovascular graft in combination with Atrium iCAST™ stents for the SMA and renal fenestrations. Use of the Zenith® Universal Distal Body Endovascular Graft is dependent on patient anatomy and physician discretion. For example, in instances where a surgically implanted graft has been previously placed in the aorta, the Zenith® Universal Distal Body Endovascular Graft may not be required if an adequate distal seal within the prior graft is obtained with the Zenith® p-Branch™. Commercially available Zenith® Spiral-Z® AAA Iliac Leg Grafts will be used. The Manufacturers' Instructions for Use should be referred to for additional information.

Standard techniques for placement of arterial access sheaths, guiding catheters, angiographic catheters, and wire guides should be employed during use of the Zenith® p-Branch™. The device and delivery system are compatible with 0.035 inch diameter wire guides.

Refer to institutional protocols relating to anesthesia, anticoagulation, access technique, and monitoring of vital signs during the procedure.

The completion imaging should be carefully interrogated for potential endoleaks as well as residual kinking/stenosis/dissection of vessels accommodated by fenestrations. Use of imaging modalities beyond conventional angiography (e.g., rotational angiography [i.e., flat-panel volume CT or cone beam CT] or IVUS) is recommended to fully assess the completeness of repair and confirm the absence of Type I and Type III endoleaks as well as stent compression or kinking/stenosis/dissection of vessels accommodated by a fenestration, especially at the distal end of a fenestration stent.

Type I and Type III endoleaks not expected to resolve with the reversal of procedural heparin warrant treatment prior to completion of the endovascular procedure. Likewise, any evidence of kinking, stenosis, or dissection of vessels accommodated by fenestrations should be resolved prior to completion of the procedure. In such cases of either Type I or Type III endoleak or residual kinking/stenosis/dissection of vessels accommodated by a fenestration, additional stenting or balloon angioplasty should be considered.

Refer to the Manufacturer's Instructions for Use for complete details regarding use of the Zenith® p-Branch™. Fluoroscopic guidance and angiography should be used throughout the procedure to verify positioning of the device with respect to patient anatomy.

7.6 Post-procedure/Follow-up

The results of the endovascular repair will be assessed by clinical and imaging evaluation intra-operatively and post-operatively, including within 30-days post-procedure, and at 6 months (180 ± 30 days), 12 months (365 ± 45 days), 2 years (730 ± 60 days), 3 years (1095 ± 60 days), 4 years (1460 ± 90 days), and 5 years (1825 ± 90 days) post-procedure according to the study schedule (Table 6.1). Follow-up windows are intended as guidelines only. They are not absolute and are not intended to limit data collection due to scheduling conflicts.

Type I and Type III endoleaks detected during follow-up warrant treatment, particularly in the setting of aneurysm growth. Type II endoleaks should be treated at the physician's discretion, depending on aneurysm behavior and size, endoleak source, and time from implantation. If the aneurysm is enlarging, treatment by embolization or ligation should be considered. Type I and Type III endoleaks should be treated with additional ballooning or prostheses.

The patency of vessels accommodated by fenestrations should be assessed at each follow-up. Additional ballooning and/or stenting may be warranted in the setting of stenosis (e.g., > 60%) or occlusion. In cases of reinterventions for stenosis/occlusion of a branch vessel targeted by a fenestration, duplex ultrasound should be performed prior to the reintervention procedure, and is suggested to be performed after the reintervention procedure, as per the standard of care for the site.

7.7 Reintervintion

Reintervention should be performed according to the institution's standard of care.

7.8 Duration of Study and Patient Participation

The total duration of patient participation is 5 years. After graft deployment, follow-up data will continue to be collected for 5 years for each patient in the clinical investigation.

7.9 Criteria and Procedures for Withdrawal

A patient may decide to withdraw from the investigation at any time either before or after undergoing the procedure without prejudice or loss of care. The patient should notify the investigator of their desire to withdraw. The investigator will notify the Sponsor. The investigator may also decide to withdraw a patient from the investigation at any time based on medical judgment. In these instances of withdrawal, data collected up to the time of patient withdrawal, including the Study Exit form shall be submitted to the Data Coordinating Center, and will include the reason why the patient has been withdrawn from the study. Any data collected on the patient up to the point of withdrawal may be used in the study.

In the event a patient is lost to follow-up or cannot be contacted for post-treatment assessments, at least three attempts will be made to locate the patient, and these efforts will be documented. If the patient cannot be located, a lost to follow-up entry will be submitted.

An autopsy, including explant of the study device, may be requested for patients who die with a study device in place. Both the excised aorta and the study device should be sent to the Data Coordinating Center for subsequent examination. Any study device excised in the course of conversion to open surgical repair should also be sent to the Data Coordinating Center. Further instructions will be provided as needed. Data will be collected and stored in a database.

7.10 Imaging

An imaging manual will be provided by the sponsor. The imaging criteria specified in the manual shall be followed for all imaging required per the CIP.

7.11 Participation Endpoints of the Study

A patient's follow-up in the study will end after any of the following:

1. Failure to deploy the device +30 days;
2. Conversion to open surgical repair +30 days;
3. Patient withdrawal or lost to follow-up;
4. Patient death;
5. Closure of the investigation; or
6. Completion of all scheduled clinical and imaging visits through 5 years.

8.0 Statistical Considerations

8.1 Hypothesis to be Tested

The primary hypothesis will assess the treatment success rate evaluated at 12 months for the Zenith® p-Branch™. [redacted] a [redacted] performance goal of 80% has been established. The performance goal will be said to have been met provided that the null hypothesis is rejected in favor of the alternative with a one-sided exact binomial test at the 0.05 level. The null (H_0) and alternative (H_A) hypotheses are expressed as follows, where π is the proportion of patients treated with the Zenith® p-Branch™ with treatment success at 12 months:

Null Hypothesis: The 12-month treatment success rate for patients treated with the Zenith® p-Branch™ does not meet the performance goal (80%).

$H_0: \pi \leq 80\%$

Alternative Hypothesis: The 12-month treatment success rate for patients treated with the Zenith® p-Branch™ meets the performance goal (80%).

$H_A: \pi > 80\%$

The safety and effectiveness of the Zenith® p-Branch™ will be established if the null hypothesis is rejected in favor of the alternative at a type I error rate of 0.05 (one-sided). This analysis will be performed on the intent-to-treat population.

8.2 Statistical Analysis

Statistical analyses will be performed using SAS® for Windows® (release 9.3 or higher) or other widely accepted statistical software. Descriptive summaries will be provided where appropriate for each of the primary and secondary endpoints. In general, summaries will be completed over the total population. Continuous variable summaries will include the number of subjects (N), mean, standard deviation, minimum, and maximum. Categorical variable summaries will include the frequency and percentage of subjects who are in the particular category. Survival analysis techniques such as Kaplan-Meier or Cox

Proportional Hazards will be incorporated if censoring of data occurs.

8.3 Sample Size Calculation

[redacted] With a clinically relevant margin of 10%, [redacted] Thirty-four (34) patients are necessary to assess the primary hypothesis, under an expected 12-month treatment success rate of 97.4% [redacted], with a one-sided exact binomial test, at a Type I error rate of 0.05 and a power of 0.8. A sample size of 80 patients will be enrolled to account for possible loss to follow-up while also ensuring sufficient use of both p-Branch graft configurations.

No more than 20 patients (i.e., 25% of total enrollment) will be enrolled at any one site [redacted]

8.4 Missing Data

Missing data will be addressed using three primary strategies: 1) estimating missing data with the best available data, 2) case deletion, and 3) multiple imputation. The first strategy may be used for missing imaging data. Previous clinical study experience suggests that some portion of the imaging data may not meet the criteria for accurate review by the core laboratory; however, it is recognized that the investigator uses this information to provide the best possible care for the patient. Therefore, it is reasonable to substitute any missing core laboratory measurements with the corresponding measurements made by the investigator or institutional staff. In addition, the absence or presence of clinical sequelae may supplement the required missing core laboratory assessment of device performance. This strategy is a best approximation of the missing data value.

The second strategy is case deletion. If the amount of missing data does not result in a reduction of analyzable patients to a number that is below that which is required for sufficient statistical power of the

primary endpoints, then case deletion will be the method of choice for that analysis.

The third method is multiple imputation. This method will be used to predict missing endpoint or covariate data for any reason, including patient lost to follow-up. It may be that the primary study endpoints depend upon certain covariates; therefore, it may be possible to model study endpoints, given a series of related covariates. This model-based imputation exercise may provide approximations of the missing data that can be utilized in estimating event rates and confidence bounds.

8.5 Site-level Poolability

Poolability of data from multiple sites will be verified by examining the primary endpoint among sites. Site-level poolability will be considered appropriate provided that this measure is similar among sites. It is expected that some sites may have too few patients to provide reasonable site-level estimates of the primary endpoint. Pooling of this information will be explored based on hospital size (annual discharge and number of beds), type of hospital (community versus teaching), and other group-wise strategies. Should one or more sites differ from the rest, then subsequent analyses will include the discriminating covariate or a covariate to distinguish between the unusual site(s) and those sites that are considered poolable.

8.6 Limitations of the Study

This study is designed as a single-arm study without a concurrent control group. The hypothesis of the study involves meeting a performance goal derived from previous clinical study results and literature. In the unlikely event that major changes in medical practice have occurred since those studies were performed, the determination of whether or not the device met the performance goal may be questioned.

Study results may be generalizable only to the types of patients enrolled in the study, which is expected to represent the Medicare patient population based on age. For a previous study, with similar inclusion and exclusion criteria, the mean was 75 years (IDE # G040063).[3]

9.0 Deviations from Clinical Investigation Plan

Investigators are not allowed to deviate from this clinical investigation plan (CIP) without prior authorization by the Sponsor except under emergency situations when necessary to preserve the rights, safety, and well-being of human subjects.

Deviations and non-compliances will be recorded together with an explanation. Deviations or non-compliances that impact the rights, welfare, or safety of patients shall be reported to the Sponsor and IRB as soon as possible.

If appropriate, corrective and preventive actions will be discussed by the sponsor, investigator, and/or the IRB to determine a suitable course of action.

10.0 Data Collection and Reporting

10.1 Electronic Case Report Forms

Patient data will be collected and entered by trained personnel at the investigative site into an electronic Case Report Forms (eCRFs) through an electronic data capturing (EDC) system.. This is a secure, web-based system that allows those with permission to access data from any location at any time. Source data are to be retained for data entered into the EDC system. Data obtained and simultaneously entered into the EDC system may also serve as source documentation (e.g. telephone follow-up). Site personnel are required to have unique login names and passwords in order to enter patient data. In accordance with 21 CFR Part 11, the EDC system creates a secure, computer-generated, time-stamped audit trail to record the date and time of operator entries and actions that create, modify, or delete electronic records.

10.2 Data Reporting

Annual progress reports and a final report at the conclusion of the clinical investigation (or if the study is terminated early) will be submitted by the investigators and the Sponsor to the regulatory bodies and IRBs as required by local regulations.

This clinical study shall be registered with the National Institutes of Health (NIH) National Library of Medicine's (NLM) ClinicalTrials.gov website. Registration and reporting of results shall be submitted in accordance with Section 801 of the Food and Drug Administration Amendments Act.

11.0 Data Management and Quality Assurance

11.1 Data Entry and Quality Assurance

Each principal investigator or appropriately trained designee shall enter the clinical data into the EDC on standardized eCRFs. Investigators will provide all applicable clinical data and documentation to the

sponsor. Patient data and documents pertaining to the study will be kept and archived by the sponsor. Data will be reviewed for missing data, data consistency, and reasonableness of responses. Discrepancies will be resolved through a formal query process involving direct contact with investigators or research coordinators. The data coordinating center is responsible for database management, data verification, data archiving and data retention.

Pertinent imaging (pre-procedure, procedure, and follow-up) will be sent to MED Institute, which will coordinate shipment of imaging for independent analysis.

11.2 Data Monitoring Arrangements

The conduct of the clinical study will be supervised through a process of centralized and on-site monitoring. The Data Coordinating Center will remotely monitor the study for data completeness and for adverse events. On-site monitoring will be implemented as necessary throughout the course of the study. The investigator/institution will provide direct access to source data/documents for study-related monitoring, audits, IRB review and regulatory inspection. Written procedures for monitoring the investigation are maintained by the monitors and can be found in Appendix B.

12.0 Safety Monitoring and Procedures for Reporting Adverse Events

12.1 Safety Monitoring

A Data Safety Monitoring Board (DSMB) consisting of independent physicians and a least one independent statistician, who are not investigators in the investigation, and who do not have a perceived conflict of interest with the conduct and administration of the investigation, will be convened on a regular basis to evaluate investigation progress and review adverse events.

An independent Clinical Events Committee (CEC) consisting of physicians, who are not investigators in the investigation, and who do not have a perceived conflict of interest with the conduct and administration of the investigation, will be established to adjudicate clinical events reported during the investigation. This adjudication will be performed to assess whether the events were due to a pre-existing or unrelated condition, or were procedure-related, technique-related, and/or device-related.

Regularly scheduled review/monitoring of all patient data will be conducted at the Data Coordinating Center, in part, for identification of adverse events and assurance that they are correctly reported to the DSMB and CEC.

12.2 Adverse Event Reporting

Adverse events are to be reported to the Data Coordinating Center using the appropriate eCRF. In cases of adverse device effects or serious adverse events, completed forms should be submitted to the Data Coordinating Center as soon as possible upon knowledge of the event.

The Data Coordinating Center will review the information submitted for possible reporting to the Sponsor. The Sponsor shall, if required according to applicable regulations, report the event to the appropriate Regulatory Authority. The Principal Investigator or designee will notify their IRB of applicable events according to institutional guidelines. If indicated, all investigators and sites will be notified of applicable by the Sponsor.

13.0 Early Termination or Suspension of the Investigation

Any decision to suspend enrollment or terminate the clinical study, either completely or at one or more clinical sites, will be made by the Sponsor and, if appropriate, the local IRB. If a decision is made to terminate the study, all patients already treated will be followed for 60 months following the procedure. Regulatory authority(ies) and/or IRB(s) will be notified as required by local regulations.

14.0 Ethical Considerations

The investigation will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and in compliance with ISO 14155, ICH GCP, 21 CFR 812, and any regional or national regulations, as appropriate.

The investigator is responsible for obtaining approval of this clinical investigation by the relevant IRB at their associated institution and the clinical investigation will not begin until a favorable opinion of the IRB .The Sponsor must be provided with a copy of this approval prior to delivery of the study device. The investigator is responsible for complying with requirements imposed by an IRB and/or regulatory authority. Furthermore, the Sponsor and the investigator will ensure that local regulations concerning data protection are followed.

Written informed consent must be obtained from all patients, or the patients' legally-authorized representative, in accordance with applicable regulatory requirements prior to enrollment in the study.

15.0 Publication Policy

Publication policy, rights, and obligations for this investigation have been negotiated, detailed, and defined in the Investigation Contractual Documents with the investigation sites and investigators.

16.0 Trial Administration and Investigators

16.1 Approvals and Agreements

The Sponsor, national principal investigator, and the principal clinical investigators for each site shall agree to this document and any modifications. A justification for any modifications will be documented. Approval and agreement will be indicated by signing and dating the appropriate document.

16.2 Investigators

To see a complete list of the Sponsor, Manufacturer, Data Coordinating Center, and Monitor, along with their contact information, please refer to Appendix A. A complete list of the national principal investigator, principal investigators and coordinating investigators, and core laboratory, along with their qualifications and contact information, will be updated and maintained by the Data Coordinating Center.

16.3 Insurance

The devices are covered by the Sponsor's product liability insurance, and a clinical investigation insurance policy will be taken out according to local requirements. Insurance for the study will be obtained by the sponsor prior to patient enrollment.

[redacted]

[redacted]

APPENDIX B – Written Procedures for Monitoring Investigations

Written Procedures for Monitoring Clinical Investigations

A. Selection of the monitor.

Designated by the Sponsor to oversee the investigation, the monitor may be an employee of Cook, an employee of a monitoring organization (CRO) or an independent contractor or consultant. The monitor shall be qualified by training and experience to monitor the investigation in accordance with all applicable regulations and standards for conducting clinical investigations.

B. General duties of the monitor.

The monitor must ensure that the investigation is conducted in accordance with:

1. The signed investigator agreement.
2. The Clinical Investigation Plan (CIP)/protocol.
3. Any conditions imposed by the IRB or Regulatory Authority.
4. The requirements of the applicable regulations and standards.

C. Reports by the monitor to the Sponsor.

1. Any noncompliance with the items listed above. In the event that the investigator is not complying with the requirements outlined above, it is the Sponsor's responsibility to secure compliance.
2. Any adverse events or effects that are potentially reportable to a Regulatory Authority.

D. Initiating the investigation.

Prior to initiating any clinical use of the device, the monitor and/or a Sponsor representative will participate in a pre-investigation or initiation visit with each investigative site.

At a minimum, the following items shall be addressed during the site initiation visit:

- Provide training to investigator on his/her responsibilities per the investigator agreement, applicable laws, regulations and standards; and
- Provide training to investigator that the IRB approval letter and informed consent/patient information is on file before initiation of the clinical investigation.

Additionally, training may be provided to the investigator on:

- The regulatory status of the device/product(s) and the requirements for the accountability of same;
- The nature of the CIP;
- The requirements for an adequate and well-controlled clinical investigation;
- His or her obligation to obtain informed consent in accordance with applicable regulations;
- His or her obligation to ensure continuing review of the clinical investigation by the IRB in accordance with conditions of approval and applicable regulations and to keep the Sponsor informed of such IRB approval and subsequent IRB actions concerning the investigation;
- The importance of access to an adequate number of suitable patients to conduct the investigation;
- The importance of adequate facilities for conducting the clinical investigation; and
- The importance of sufficient time from other obligations to carry out the responsibilities to which the investigator is committed by applicable regulations.

E. During the course of the investigation, at the direction of the Project Manager, the monitor should visit the site frequently enough to ensure that:

- The facilities and research staff used by the investigator continue to be acceptable for purposes of the clinical investigation;
- The applicable version of the CIP and agreements are being followed;
- Changes to the CIP, informed consent/patient information have been approved by the IRB and/or reported to the Sponsor and the IRB;
- Accurate, complete, and current records are being maintained;
- Accurate, complete, and timely reports are being made to the Sponsor and IRB; and
- The investigator is carrying out the agreed-upon activities and has not delegated them to other previously unspecified staff.

As appropriate, the following tasks could be performed during periodic visits:

- Device/product accountability review;
- Adverse event review to ensure that events are appropriately reported within the time periods required by the Sponsor, CIP, IRB, and applicable regulatory requirements; and
- Source data verification per the monitoring plan to determine that :

- Informed consent/patient information has been documented in accordance with applicable regulations and expectations of local IRB;
- The information recorded in the CRFs (paper or electronic) is complete, accurate, and legible;
- There are no omissions in the CRFs of specific data elements, such as the administration to any patient of concomitant test articles or the development of an intercurrent illness;
- Missing visits or examinations are noted; and
- Patients failing to complete the clinical investigation and the reason for each failure are noted.

F. Records of the monitor.

The monitor shall prepare and maintain records of each initiation visit and each periodic visit, general site contact, or discussion. These will include:

1. Date, name and address of the investigator, and names of other staff members present at each meeting.
2. A summary of the findings of the visit.
3. A statement of any action taken by the monitor or investigator to correct any deficiencies noted.
4. The monitor shall immediately notify the Sponsor of any conditions of non-compliance with the Clinical Investigation Plan, conditions of IRB or Regulatory Authority approval, or the applicable regulations.

APPENDIX C – Definitions

Adverse device event:

Adverse event related to the use of an investigational medical device.

Adverse event:

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.

Barb separation:

Radiographic evidence of detachment of barbs from the stent strut.

Calcification:

Calcification will be graded based upon the following:

- None: Lack of calcification;
- Mild: Less than 40% circumferential calcification;
- Moderate: 40-70% circumferential calcification;
- Severe: Greater than 70% circumferential.

Clinical utility measures:

Amount of contrast used during index procedure, radiation dose, procedure time, days to resumption of oral fluids, duration of ICU stay, days to discharge.

Clinically significant migration (stent-graft):

Antegrade or retrograde movement of the stent-graft requiring surgical or endovascular intervention.

Clinically significant migration (stent):

Antegrade or retrograde movement of any fenestration stent requiring surgical or endovascular intervention.

Device deficiency:

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling.

Disabling chronic obstructive pulmonary disease (COPD):

Having a forced expiratory volume (FEV_1) <1.0 liter or receiving home oxygen therapy.

Embolization:

Clinical evidence of ischemic tissue remote from the operative field, presumably caused by thrombus dislodged from the aneurysmal sac, aortic neck, or adjacent vessels, including ischemia of the kidneys, pelvis (IIA), or lower limbs. This is, of course, distinct from intentional pre-operative, operative, or post-operative embolization procedures.

Estimated glomerular filtration rate (eGFR):

A measure of kidney function based on serum creatinine, age, race, and gender that is used to determine stage of chronic kidney disease.

Limb occlusion:

The presence of thrombus within one or both graft limbs (including any legs and extensions) creating occlusion.

Major complications:

Occurrence of any of the following: death, aneurysm rupture, or conversion to open surgical repair; renal failure requiring dialysis; bowel obstruction, bowel ischemia, or aorto-enteric fistula; stroke; paralysis.

Medically intractable hypertension:

Having a systolic arterial pressure >160 mmHg despite receiving medication.

MI (Non-Q-Wave):

Investigator-identified patients having clinical evidence of a myocardial infarction with elevated peak CK values greater than or equal to three times the upper limit of normal with elevated CK-MB (above

the institution's upper limit of normal) in the absence of new pathological Q-waves or clinical evidence of a myocardial infarction with troponin greater than three times the upper limit of normal, as determined by the investigator.

MI (Q-Wave):

Post-procedure presence of new Q-waves greater than 0.04 seconds in at least two EKG leads.

New York Heart Association Classification:

1 Patient with cardiac disease but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea.

2 Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest, ordinary physical activity results in fatigue, palpitation or dyspnea.

3 Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest, less than ordinary physical activity causes fatigue, palpitation or dyspnea.

4 Patients with cardiac disease resulting in inability to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Occlusive disease of iliac arteries:

Occlusive disease will be graded based upon the following:

- None: Lack of occlusive disease;
- Mild: Some disease, focal with less than 30% narrowing;
- Moderate: Between 30-50% narrowing not requiring interventional techniques to meet entry criteria;
- Severe: Greater than 50% or any patient requiring angioplasty prior to endograft delivery.

Procedural duration:

Incision time to closure time.

Proximal sealing zone:

Non-aneurysmal aortic segment from the distal margin of the SMA to the proximal extent of the graft.

Radiographic migration (stent-graft):

Antegrade or retrograde movement of the stent-graft ≥10 mm relative to anatomical landmarks identified on the first post-operative CT scan.

Radiographic migration (stent):

Antegrade or retrograde movement of a fenestration stent ≥10 mm within the stented artery as compared to the position on the first post-operative CT scan.

Renal failure:

Acute or progressive renal insufficiency leading to the need for dialysis or hemofiltration.

Renal insufficiency:

A rise in serum creatinine of more than 30% above the pre-procedure level, resulting in a serum creatinine level >2.0 mg/dl (176.8 µmol/L) that does not spontaneously resolve (does not include those patients with a pre-procedure serum creatinine >2.0 mg/dl [176.8 µmol/L]).

Severe adverse device event:

An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Serious adverse event (SAE):

An 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.

Stent/attachment system fracture/break:

Fracture or breakage of any portion of the stent or attachment system including metallic fracture or breakage of any suture material used to construct the stent or secure the stent or attachment system to the graft material.

Technical success:

Successful access of the aneurysm site and deployment of the Zenith® p-Branch™ endovascular graft in the intended location. The endovascular graft and all vessels targeted with fenestrations must be patent at the time of deployment completion as evidenced by intraoperative angiography.

Tortuosity of iliac arteries will be graded based upon the following:

- None: Lack of tortuosity;
- Mild: Fairly straight arteries;
- Moderate: Angulation manageable with stiff wires (<70°);
- Severe: Angulation difficult, may require surgical exposure for straightening, not straightened entirely with wires.

Treatment success:

Technical success and freedom from all of the following at 12 months:

- Type I or Type III endoleaks that require intervention post-discharge (including Type I and Type III endoleaks identified for treatment on the 12-month follow-up CT);
- Aneurysm growth > 0.5 cm;
- AAA related serious adverse events (i.e. death, rupture, or conversion to open surgical repair) as adjudicated by an independent CEC;
- AAA-related major complications (i.e., renal failure requiring permanent dialysis; bowel obstruction, ischemia, or fistula; stroke with permanent deficit; or paralysis) as adjudicated by an independent CEC.

Type Ia endoleak:

A leak occurring at the proximal fixation zone of the stent-graft.

Type Ib endoleak:

A leak occurring at the distal fixation zone of the stent-graft.

Type Ic endoleak:

A leak occurring at the distal fixation zone of the covered stents in the visceral vessels incorporated by the fenestrations.

Type II endoleak:

A leak caused by retrograde flow from patent lumbar arteries, inferior mesenteric artery, or other collateral vessels.

Type III endoleak:

A leak caused by a defect in the graft fabric, or inadequate seal of modular graft components including leakage around fenestrations in the case of covered stents in visceral vessels incorporated by the fenestrations.

Type IV endoleak:

A leak caused by graft fabric porosity, often resulting in a generalized blush of contrast within the aneurysm sac.

Endoleak (early):

Any endoleak observed within 30 days of device deployment.

Endoleak (late):

Any endoleak observed later than 30 days after device deployment that was not documented during the first 30 days post-deployment.

Unanticipated serious adverse device event:

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.