SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Endovascular Graft

Device Trade Name: Cordis INCRAFT® AAA Stent Graft System

Device Procode: MIH

Applicant's Name and Address: Cordis Corporation
1820 McCarthy Boulevard
Milpitas, CA, 95035 U.S.A

Date of Panel Recommendation: June 12, 2018

Premarket Approval Application (PMA) Number: P150002

Date of FDA Notice of Approval: 11/27/2018

II. INDICATIONS FOR USE

The INCRAFT® AAA Stent Graft System (INCRAFT) is intended for the endovascular treatment of patients with infrarenal abdominal aortic aneurysms with the following characteristics:

- Adequate, but complex iliac or femoral vessel morphology (e.g., high tortuosity index, heavily calcified, small diameter), that is compatible with vascular access techniques, devices or accessories;
- Proximal neck length ≥ 10 mm;
- Aortic neck diameters ≥ 17 mm and ≤ 31 mm;
- Aortic neck suitable for suprarenal fixation;
- Infrarenal and suprarenal neck angulation ≤ 60°;
- Iliac fixation length ≥ 15 mm;
- Iliac diameters ≥ 7 mm and ≤ 22 mm; and
- Minimum overall AAA treatment length (proximal landing location to distal landing location) ≥ 128 mm.

III. CONTRAINDICATIONS

The INCRAFT® AAA Stent Graft System is contraindicated in the following patient populations:

- Patients with a known allergy or intolerance to the device materials [i.e., nickel titanium (nitinol), polyethylene terephthalate (PET), polytetrafluoroethylene (PTFE), tantalum, or platinum-iridium alloy].
- Patients who have a condition that threatens to infect the graft.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Cordis INCRAFT® AAA Stent Graft System labeling.

V. DEVICE DESCRIPTION

The INCRAFT® AAA Stent Graft System (also referred to as INCRAFT) is a modular bifurcated endovascular stent graft system comprised of two main types of devices: the INCRAFT® Stent Graft implant and the INCRAFT® Delivery System. The stent graft is preloaded into the delivery system and advanced to the intended location under fluoroscopy, where it is deployed to create a new blood flow channel to exclude an aneurysm.

Stent Graft

The INCRAFT consists of three main components (**Figure 1**): an aortic bifurcate prosthesis and two iliac limb prostheses. In addition, to extend the implant in a caudal direction, the iliac limb prosthesis can be used as an iliac extension prosthesis. Each prosthesis is constructed of a seamless, woven polyester graft supported by a series of short, laser-cut, electro-polished, self-expanding nitinol stent-rings throughout the entire length. Aortic bifurcate and iliac limb prosthesis sizes, their sizing recommendations and corresponding delivery system profiles are described in **Table 1** and **Table 2**.

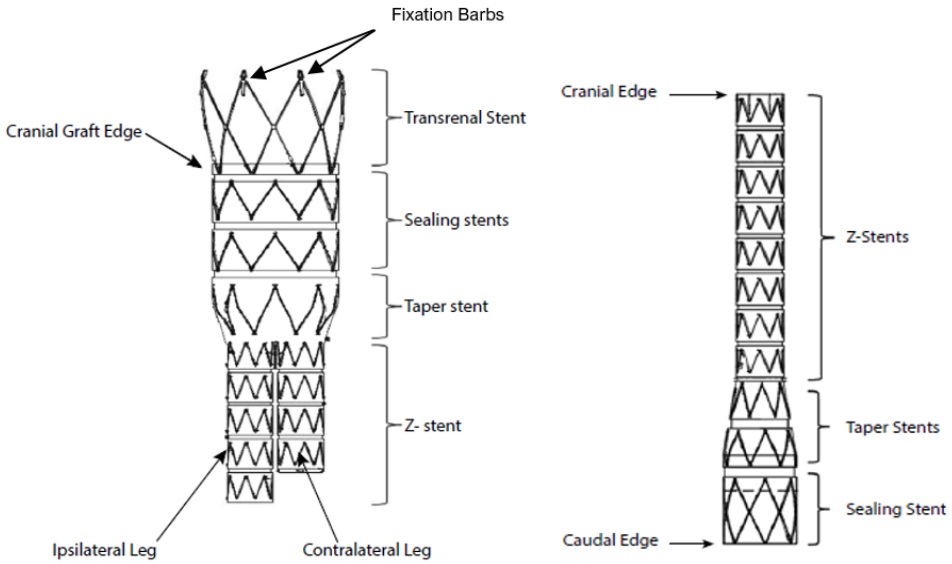


Figure 1: INCRAFT Aortic Bifurcate and Iliac Limb/ Iliac Limb Extension

The aortic bifurcate prosthesis is deployed first into the cranial portion of the infrarenal aorta, as well as a small portion of the suprarenal aorta. It has a flared bare transrenal stent with 8 or 10 laser-cut barbs depending on the cranial diameter. The fixation barbs (**Figure 1**) are located at the cranial end of the transrenal stent and help keep the prosthesis in place.

Distal to the bare transrenal stent, the main trunk of the aortic bifurcate prosthesis has two sealing stents and a taper stent that divides into the ipsilateral and contralateral legs,

supported by a series of Z-stents. While the diameter of the trunk varies by product code, the lengths of the trunk (49 mm) and legs (45 mm on the ipsilateral side and 37 mm on the contralateral side), as well as the diameters of the legs (11 mm) are constant. The aortic bifurcate prosthesis is manufactured in 4 trunk diameter sizes (22, 26, 30 and 34 mm).

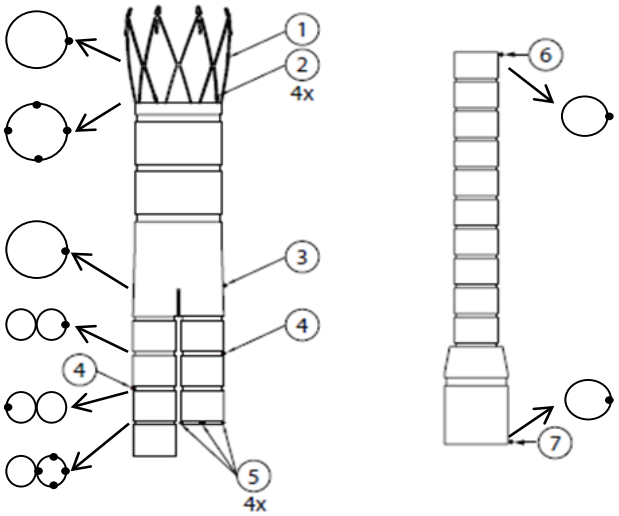
The iliac limb prostheses are deployed into the legs of the aortic bifurcate prosthesis and into the ipsilateral and contralateral iliac vessels. The overlap between the aortic bifurcate prosthesis and the iliac limb prosthesis can vary between 2 cm and 5 cm on the ipsilateral side, and between 2 cm and 4 cm on the contralateral side.

The iliac limb prosthesis has a series of Z-stents cranially, 1 or more taper stents (if other than a straight configuration), and a diamond sealing stent caudally. The cranial diameter is always constant at 13 mm while the length and the caudal diameter of the iliac limb prosthesis could vary by product code. The iliac limb prostheses are available in 5 different caudal diameters (10, 13, 16, 20 and 24 mm) and in 4 different lengths (8, 10, 12, and 14 cm) except for the 24 mm x 8 cm code that does not exist.

The iliac limb prostheses could also be used as iliac extensions by placing one into a previously deployed iliac limb prosthesis to gain additional exclusion length.

> **Note:** The 10 mm iliac limb prosthesis cannot be extended by design as the cranial diameter for all iliac limb prostheses is 13 mm.

Radiopaque markers provide a reference for proper alignment when deploying the prosthesis components (**Figure 2**). The aortic bifurcate cranial edge markers indicate the location of the cranial edge of the graft material (0.0-1.0 mm below the markers). The cranial edge markers serve as a guide for placement of the bifurcate's cranial edge just the below the lowest renal artery. The contralateral side marker indicates the orientation of the bifurcate's contralateral leg. The bifurcate's maximum and minimum overlap markers indicate the overlap range allowed for the cranial end of the iliac limb prostheses within each leg of the aortic bifurcate. The contralateral gate markers represent the caudal end of the bifurcate's contralateral leg and provide visualization in three dimensions to assist in cannulation of the the contralateral leg. Radiopaque markers on the iliac limb protheses are included to indicate cranial and caudal edges of the graft and to assist in placement within the bifurcate leg cranially and iliac landing zone caudally.



Marker	Material	Configuration
1. Contralateral side marker	Tantalum	Cylindrical marker crimped onto stent strut
2. Bifurcate cranial edge markers	Tantalum	Cylindrical marker crimped onto stent strut. Graft edge begins below and within 1 mm of the bottom edge of the marker.
3. Maximum overlap marker	Platinum-Iridium alloy	Cylindrical markers sewn onto the graft
4. Minimum overlap marker	Platinum-Iridium alloy	Cylindrical markers sewn onto the graft
5. Contralateral leg-gate markers	Platinum-Iridium alloy	Cylindrical markers sewn onto the graft edge
6. Limb cranial edge marker	Tantalum	Cylindrical marker crimped on the stent strut
7. Limb caudal edge marker	Tantalum	Cylindrical marker crimped on the stent strut

Figure 2: INCRAFT Prothesis Markers

Table 1: INCRAFT Aortic Bifurcate Prosthesis Sizes and Sizing Guide

Product Code	Bifurcate Main Diameter (mm)	Aortic Vessel Diameter Range Treated (mm)	Delivery System ID (F)	Delivery System OD		Ipsilateral Length (cm)	Contralateral Length (cm)
				F	mm		
AB2298US	22	17.0 - 19.9	13	14	4.7	9.4	8.6
AB2698US	26	20.0 - 22.9	13	14	4.7	9.4	8.6
AB3098US	30	23.0 - 26.9	13	14	4.7	9.4	8.6
AB3498US	34	27.0 - 31.0	15	16	5.3	9.4	8.6

Table 2: Iliac Limb and Limb Extension Prosthesis Sizes and Sizing Guide

Product Code	Limb Diameter (mm)	Iliac Vessel Diameter Range Treated (mm)	Limb Length (cm)	Delivery System OD		Ipsilateral Treatment Length (mm)	Contralateral Treatment Length (mm)
				F	mm		
IL1008US	10	7.0 - 8.9	8.2	12	4.0	128-156	128-147
IL1010US	10	7.0 - 8.9	10.1	12	4.0	147-175	147-166
IL1012US	10	7.0 - 8.9	12.0	12	4.0	166-194	166-185
IL1014US	10	7.0 - 8.9	13.8	12	4.0	184-212	184-203
IL1308US	13	9.0 - 10.9	8.2	12	4.0	128-156	128-147
5IL1310US	13	9.0 - 10.9	10.1	12	4.0	147-175	147-166
IL1312US	13	9.0 - 10.9	12.0	12	4.0	166-194	166-185
IL1314US	13	9.0 - 10.9	13.8	12	4.0	184-212	184-203
IL1608US	16	11.0 - 13.9	8.2	12	4.0	128-156	128-147
IL1610US	16	11.0 - 13.9	10.1	12	4.0	147-175	147-166
IL1612US	16	11.0 - 13.9	12.0	12	4.0	166-194	166-185
IL1614US	16	11.0 - 13.9	13.8	12	4.0	184-212	184-203
IL2008US	20	14.0 - 17.9	8.2	12	4.0	128-156	128-147
IL2010US	20	14.0 - 17.9	10.1	12	4.0	147-175	147-166
IL2012US	20	14.0 - 17.9	12.0	12	4.0	166-194	166-185
IL2014US	20	14.0 - 17.9	13.8	12	4.0	184-212	184-203
IL2410US	24	18.0 - 22.0	10.1	13	4.3	147-175	147-166
IL2412US	24	18.0 - 22.0	12.0	13	4.3	166-194	166-185
IL2414US	24	18.0 - 22.0	13.8	13	4.3	184-212	184-203

Delivery System

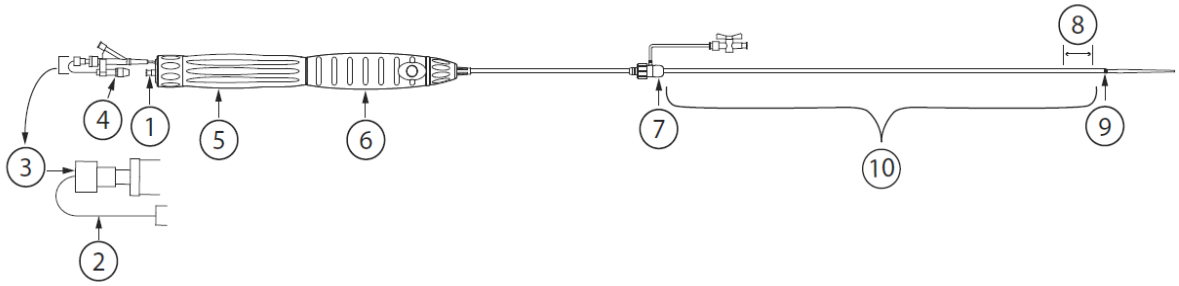
Each prosthesis is loaded into a delivery system (**Figure 3**) intended to facilitate controlled deployment of the prosthesis into the intended locations under fluoroscopic guidance. Each delivery system is delivered over a 0.035" (0.89 mm) stiff guide wire and is operated to deploy the prosthesis by rotating the gold handle component (#5 in **Figure 3**) in a clockwise direction while firmly holding the white handle component (#6 in **Figure 3**). The deployment of each prosthesis is completed by pulling a secondary release mechanism (#4 in **Figure 3**).

There are two variations of the delivery system: one for the aortic bifurcate prosthesis, and one for the iliac limb prosthesis. Both variations of the delivery system are disposable and for single use only.

The aortic bifurcate delivery system has an integrated sheath introducer along with a hemostatic valve to facilitate component exchanges during the procedure. The working length of the aortic bifurcate delivery system is approximately 54 cm. The size of the integrated sheath introducer varies depending on the diameter of the prosthesis it contains. For prosthesis diameters of 22, 26, and 30 mm, the inner diameter of the integrated sheath introducer is 13F (outer diameter of 14F). For the prosthesis diameter of 34 mm, the inner diameter of the integrated sheath introducer is 15F (outer diameter of 16F). The outer surface of the integrated sheath introducer has a lubricious (hydrophilic) coating at the distal end to facilitate introduction into the vasculature. The graft is held between the inner and the outer

catheter of the delivery system, just proximal of the distal catheter tip. The inner catheter is 0.035” guidewire compatible terminating in the tapered catheter tip.

The delivery system of the iliac limb prosthesis is similar to that of the aortic bifurcate except for its size, and that it does not have an integrated sheath introducer. The iliac limb delivery system has a working length of approximately 77 cm and can be delivered through the integrated sheath introducer of the aortic bifurcate system. The iliac limb delivery system has a 12F outer diameter for prosthesis diameters between 10 mm and 20 mm, and a 13F outer diameter for the 24 mm diameter prosthesis. The outer surface of each iliac limb delivery system has a lubricious (hydrophilic) coating at the distal end to facilitate introduction into the vasculature. The graft is held between the inner and the outer catheter of the delivery system, just proximal of the distal catheter tip. The inner catheter is 0.035” guidewire compatible terminating in the tapered catheter tip.



1. Manifold assembly (manifold core with guidewire lumen flush connector and manifold shell)
2. Fixation release wire
3. Fixation release wire hemostasis valve
4. Release wire retainer
5. Gold handle component (body)
6. White handle component
7. Sheath hemostasis valve (aortic bifurcate only)
8. Prosthesis location
9. Sheath tip marker
10. Integrated sheath introducer (aortic bifurcate only)

Figure 3. INCRAFT Delivery System Components

Please refer to the Cordis INCRAFT® AAA Stent Graft System Instructions for Use for additional description on the implants and associated delivery systems.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for the treatment of infrarenal abdominal aortic aneurysms, including endovascular repair using other endovascular grafts, medical management, and open surgical repair. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The INCRAFT is marketed in the European Union (Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Liechtenstein, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, United Kingdom), the Middle East (Egypt, Israel, Kuwait, Saudi Arabia, United Arab Emirates), Canada, South America (Argentina, Brazil, Colombia, Mexico), and Asia Pacific (Australia, China, Korea). The INCRAFT has not been withdrawn from the market in any country for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

In **Table 3** below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

Table 3: Potential Adverse Events

• Amputation • Anesthesia complications • Aneurysm enlargement • Aneurysm sac rupture • Aortic damage (perforation, dissection, bleeding, rupture) • Aortocaval fistulae • Aortoenteric fistulae • Arterial or venous thrombosis • Bleeding events • Bowel complications (e.g., ileus, transient ischemia, infarction, necrosis) • Cardiac arrhythmia • Cardiac complications • Cardiac failure or infarction • Claudication • Coagulopathy • Component migration • Contrast toxicity / anaphylaxis • Death • Edema • Embolism or thrombotic events	• Endoleaks • Fever • Gastrointestinal complications • Genitourinary complications (e.g., ischemia, erosion, fistula, incontinence, hematuria) • Graft erosion • Graft material wear • Graft puncture • Graft twisting or kinking • Hematoma (surgical) • Hepatic failure • Impotence • Improper stent graft placement • Incomplete stent graft deployment • Infection • Insertion and removal difficulties • Lymphatic complications • Multiorgan system failure • Neurological complications (e.g. CVA, transient ischemic attack)	• Open surgical conversion • Paralysis or paraparesis • Perigraft flow • Post-implant syndrome • Prosthesis occlusion/stenosis • Pseudoaneurysm • Pulmonary complications • Radiation complications • Renal failure/renal insufficiency • Sheath leakage • Shock • Stenosis/occlusion of native vessel • Stent fracture / separation / dislodgement of stent strut • Suture break (endograft) • Vascular access site complications occlusion/stenosis • Vascular spasm/trauma • Wound complications

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

IX. SUMMARY OF NONCLINICAL STUDIES

The following studies were completed to evaluate the INCRAFT device: non-clinical bench testing, biocompatibility, sterilization/packaging/shelf-life, and animal studies. These are discussed in more detail in the subsequent sections.

A. Laboratory Studies

The INCRAFT underwent testing for design verification and validation, including long-term durability and corrosion testing. All testing was conducted in accordance with international standards and guidance documents, specifically ISO 25539-1 "Cardiovascular implants -- Endovascular devices -- Part 1: Endovascular prostheses" and ISO 7198 "Cardiovascular implants and extracorporeal systems -- Vascular prostheses -- Tubular vascular grafts and vascular patches." Testing was conducted on either a subset of device configurations/sizes for each test or worst-case sizes, in order to represent the entire size range available for the INCRAFT.

The testing details provided below include results from baseline, as well as 2 year accelerated aging, as appropriate. An asterisk (*) inciates that testing was performed at both baseline and 2 years accelerated aging. A summary of this testing is provided in **Table 4**.

Table 4: Summary of Design Verification and Validation Testing

Test Name	Test Purpose	Acceptance Criteria	Results
Delivery System Testing			
Dimensional Verification and Component Dimensions Compatibility	To determine the working length of INCRAFT delivery system	All test samples must meet predefined specification for working length (90% of the population with 95% confidence)	Pass*
	To confirm that the INCRAFT delivery system is compatible with a 0.035" guide wire	All test samples must accept a typical 0.035" stiff guide wire through the entire length of the delivery system's guide wire lumen	Pass
	To confirm compatiblility of distal sheath section of bifurcate delivery system with limb delivery system	The inner diameter of the bifurcate distal sheath must be ≥ 4.0 mm and all test samples must meet a limb delivery system compatibility force with the bifurcate distal sheath of ≤ 10.0 lbf (90% of the population with 95% confidence)	Pass*
	To confirm luer compatibility with accessory devices	All test samples must meet predefined specification for luer dimensions	Pass*
Profile/ Diameter Test	To determine the profile of INCRAFT delivery system	All test samples must meet its nominal labeled profile ≤ 4.8 mm (22, 26 & 30 mm bifurcate) ≤ 5.5 mm (34 mm bifurcate) ≤ 4.2 mm (10, 13, 16 & 20 mm limbs) ≤ 4.5 mm (24 mm limb) (90% of the population with 95% confidence)	Pass*
Assessment of Hemostasis	To confirm ability of sheath valve to maintain hemostatic seal	All test samples must meet a maximum leak rate of ≤ 60 ml/min (90% of the population with 95% confidence)	Pass*
Simulated Use Models	Design validation tests to evaluate: (a) ability to flush guidewire lumen; (b) accessory compatibility; (c) delivery system chemical compatibility; (d) device deliverability and deployment; (e) prosthesis conformability and kink resistance	All test samples must be able to complete flushing of the guidewire lumen and without incident	Pass
		All test samples must show acceptable balloon compatibility during tracking activities and post deployment shall be assessed	Pass
		All test samples must pass a subjective assessment of the delivery system kink resistance as determined by the test performer.	Pass
		All test samples must not show visible signs of crazing, cracking, blister/ bubble, haze/ cloudiness, pitting, discoloration, precipitate formation or other conditions	Pass
		All test samples must pass a subjective, simulated use assessment of deployment accuracy as determined by the test performer.	Pass
		All test samples must have a deployment initiation torque of ≤ 1.75 rotations of the handle	Pass
		All test samples must meet a handle rotation angle for response of the delivery system tip of ≤ 90 degrees	Pass
		All test samples must meet a peak push force of ≤10.0 lbf	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
		All samples must pass a subjective, simulated use assessment of the prosthesis kink resistance as assessed by the test performer.	Pass
		All samples must pass a subjective, simulated use assessment of the prosthesis conformability to the vessel as assessed by the test performer.	Pass
Gasket Retention	To confirm that gasket remains secure in hemostasis valve after withdrawal of inner member	All test samples must pass a gasket retention assessment to confirm that the gasket remains secure after inner member is withdrawn from distal sheath of bifurcate delivery system	Pass*
Residual Retraction Length	To confirm residual travel capability of outer member after prosthesis deployment	All test samples must meet a residual retraction length of ≥ 12.0 mm (bifurcate) / 37.0 mm (limb) (99% of the population with 95% confidence)	Pass*
Force to Deploy	To determine the force to deploy the endovascular prosthesis under simulated anatomical conditions. All applicable steps of the deployment process were evaluated	All test samples must meet a peak initiation torque of ≥ 12.0 in-oz (99% of the population with 95% confidence)	Pass*
		All test samples must meet a peak primary deployment torque of ≤ 24.0 in-lb (99% of the population with 95% confidence)	Pass*
		All test samples must meet a primary deployment force of < 26.0 lbf (99% of the population with 95% confidence)	Pass*
		All test samples must meet a secondary release force (Sheathed) of ≥ 1.6 lbf (99% of the population with 95% confidence)	Pass*
		All test samples must meet a secondary release force (Unsheathed) of ≤ 10.0 lbf (99% of the population with 95% confidence)	Pass*
Tensile Bond Strength	To confirm adequate tensile bond strengths of delivery system during delivery, deployment and retraction from the vasculature	All test samples must meet an inner member tip to hypotube tensile strength of ≥ 10.0 lbf (99% of the population with 95% confidence)	Pass*
		All test samples must meet an inner member wire guide to hypotube tensile strength of ≥ 25.0 lbf (bifurcate) and ≥ 17.0 lbf (limb) (99% of the population with 95% confidence)	Pass*
		All test samples must meet an eyelet wires to wire holder tensile strength of ≥ 1.3 lbf (99% of the population with 95% confidence)	Pass*
		All test samples must meet a bifurcate release wire to wire holder tensile strength of ≥ 5.0 lbf (99% of the population with 95% confidence)	Pass*

Test Name	Test Purpose	Acceptance Criteria	Results
		All test samples must meet proximal inner member component joint tensile strength of ≥ 10.0 lbf (95% of the population with 95% confidence)	Pass*
		All test samples must meet an outer member proximal shaft to handle tensile strength of ≥ 26.0 lbf (99% of the population with 95% confidence)	Pass*
		All test samples must meet hemostasis valve tensile strength of ≥ 35.0 lbf (99% of the population with 95% confidence)	Pass*
Torsional Bond Strength	To confirm adequate torsional bond strengths of delivery system during delivery, deployment and retraction from the vasculature	All test samples (bifurcate) must meet an inner member to hypotube torque of ≥ 3.5 in-oz (99% of the population with 95% confidence)	Pass*
		All test samples (limb) must meet an inner member to hypotube torque of ≥ 0.9 in-oz (99% of the population with 95% confidence)	Pass*
		All test samples must meet an outer member shaft to handle torque of ≥ 13.0 in-oz (99% of the population with 95% confidence)	Pass*
		All test samples (bifurcate) must meet a haemostasis valve torque of ≥ 13.0 in-oz (99% of the population with 95% confidence)	Pass*
		All test samples (bifurcate) must meet a prosthesis retention torque of ≥ 2.6 in-oz (99% of the population with 95% confidence)	Pass*
Coating Lubricity	To confirm adequate lubricity due to coating on delivery system	The tip and outer member of all test samples must have a pull force of ≤ 376 g (90% of the population with 95% confidence)	Pass*
Implant Testing			
Dimensional Verification	To determine the endovascular prosthesis diameter in the deployed state	All test samples (aortic bifurcate) must meet an outer diameter that is +/-5% of the nominal diameter after a 24 hour soak at 37°C (99% of the population with 95% confidence) All test samples (limb) must meet an outer diameter that is between the maximum labeled treatable vessel diameter (immediately after deployment) and +5% of the nominal diameter (for 24 mm limb) or +1.0 mm greater than the nominal diameter for all other limbs after a 24 hour soak at 37°C (99% of the population with 95% confidence)	Pass*
Water Permeability	To determine graft permeability	All test samples must have a water permeability of ≤ 700 ml/min/cm^2 (95% of the population with 95% confidence)	Pass*
Graft Circumferential Strength	To determine the circumferential strength of the graft material	All test samples must meet a circumferential tensile strength of ≥ 2.3 lbf/cm (99% of the population with 95% confidence)	Pass*

Test Name	Test Purpose	Acceptance Criteria	Results
Flex/ Kink	To confirm that the endovascular prosthesis can accommodate a minimum radius without kinking	All test samples (bifurcate) must meet a minimum radius of curvature of ≤ 38.1 mm (centerline radius of curvature)	Pass
		All test samples (limb) must meet a minimum radius of curvature of ≤ 25.4 mm (inner line radius of curvature)	Pass
Graft Longitudinal Tensile Strength	To determine the longitudinal tensile strength of the graft material	All test samples must meet a maximum graft longitudinal tensile force of ≥ 10.0 lbf (99% of the population with 95% confidence)	Pass*
Migration Resistance	To evaluate the ability of the endovascular prosthesis to resist migration when subjected to an axial force or pressure	All test samples must have a displacement of ≤ 10 mm for forces of: 2.24 lbf (22, 26 and 30 mm bifurcates) 2.70 lbf (34 mm bifurcate) (99% of the population with 95% confidence)	Pass*
Pull Test for Modular Components (Or Overlapping Endoprostheses)	To determine the force required to separate overlapping modular components (e.g., main body & limbs, limb & limb) in the deployed state	All test samples must meet a peak modular junction force of ≥ 0.6 lbf (99% of the population with 95% confidence)	Pass*
Radial Force	To determine the outward force as a function of the diameter of the endovascular prosthesis	All test samples must meet a maximum chronic outward force (COF) of ≤ 3.58 lbf for the smallest labeled vessel diameter after 24 hour exposure to 37°C water	Pass
		All test samples (bifurcate) must meet a minimum COF for the largest label vessel diameter (after 24 hour exposure to 37°C) of ≥ 0.50 lbf (99% of the population with 95% confidence)	Pass*
		All test samples (limb) must meet a minimum COF for the largest label vessel diameter immediately after deployment of ≥ 0.20 lbf	Pass
Strength of Graft to Stent/ Attachment System Bond	To determine the strength of the connection(s) between the graft material and discrete implant components	All samples must meet a peak force to complete separation of an internal stent to graft of ≥ 0.02 lbf (99% of the population with 95% confidence)	Pass*
		All test samples must meet a peak force to complete separation of a transrenal stent to graft of ≥ 15.0 lbf (99% of the population with 95% confidence)	Pass*
		All test samples must meet a peak marker band tensile force of ≥ 0.1 lbf (99% of the population with 95% confidence)	Pass*
Corrosion Assessment	To evaluate the corrosion resistance properties of the INCRAFT nitinol laser-cut stents	For all test samples the average breakdown potential (Eb) of the INCRAFT samples shall be greater than or equal to that of the comparison AAA device	Pass
		No preference for pitting near dissimilar material contact points in all test units that have dissimilar material contact points for the stents tested for pitting and crevice corrosion	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
MRI Compatibility	To provide the recommended scan conditions for use with the device	Non-clinical tests of the stent-graft prosthesis for MRI compatibility and safety were conducted at worst-case conditions for: displacement and deflection force; torque force; RF heating; and MRI artifact. The testing demonstrated that INCRAFT is MR Conditional. It can be scanned safely in both 1.5 Tesla (T) and 3T magnetic resonance systems under the following conditions: • Static magnetic field of 1.5T or 3T • Spatial gradient field ≤ 2500 Gauss/cm (25T/m) • Maximum whole-body-averaged specific absorption rate (SAR) of 4 W/kg for 15 minutes of scanning (First Level Controlled Mode)	Pass
Stress/Strain Analysis and Fatigue Analysis (FEA)	Determine stent strains during crimping and *in-vivo* cyclic loading conditions (radial fatigue and axial fatigue conditions). Use strain-life data to predict fatigue safety factors	The fatigue safety factor for each stent shall be ≥ 1.0 under both radial fatigue and axial fatigue loading	Pass
Fatigue and Durability Testing	Pulsatile Fatigue Testing: Evaluate the long-term durability of stent-graft assembly across 400 million cycles of pulsatile loading	All test samples must meet the following: 1. Stent Fracture: No strut fractures unless analysis of final design negates the impact of specific strut fractures on migration, sealing and/ or embolic events 2. Fabric Holes: No holes or fabric abrasions yielding a hole with a major axis >1.34 mm in length 3. Graft Attachment Separation: No stent or radiopaque marker separation from the graft that can enter the blood stream 4. Suture Breaks: Suture breaks that lead to separation of a stent from the graft will constitute failure	Pass
	Migration Durability in a Bent Neck Condition: Evaluate the long-term durability of stent-graft assembly (including fatigue performance of barbs and transrenal stent to graft attachment) under cyclic axial loads	All test samples must meet the following: 1. No point on the cranial graft edge should migrate in excess of 7 mm through the test 2. No separation of any transrenal stent apex from the graft edge 3. The tensile force to remove the transrenal stent from the graft exceeds 15 lbs	Pass
	Dynamic Modular Junction Testing: Evaluate the junction between the modular components when subjected to dynamic tensile conditions	The modular junctions include both bifurcate leg to limb junction as well as limb to limb junction. For all test samples, the stabilization of the junction must be demonstrated and there must be no complete modular separation	Pass

* Testing successfully repeated after shelf life exposure.

Fracture Root Cause Investigation

As described below, the INCRAFT was evaluated in the INSPIRATION clinical study. During the clinical study, transrenal stent fractures were observed. An investigation was conducted to identify the root cause for transrenal stent strut fractures observed in the INSPIRATION clinical study and to characterize potential risks associated with these fractures. All stent strut fractures observed in the INSPIRATION study were located at the transrenal stent component, with the majority of the fractures at the stent "Cranial X" location (**Figure 6** in **Section X.D.2.2.8**). Additionally, no transrenal stent strut fractures were observed during design verification and validation tests or the implant durability tests discussed in **Table 4.**

The root-cause investigation revealed that the primary cause of the strut fractures was likely cardiac-induced cyclic axial deformations (i.e., axial length changes in the transrenal aortic region associated with the cardiac cycle). To support the root cause analysis, a range of axial compression values was determined to use as boundary conditions to input into a finite element analysis (FEA). These values were obtained from literature sources, clinical data of patients with the INCRAFT device (i.e., dynamic CT imaging in one patient after exhibiting fractures for one quantitative measurement, post-procedural imaging for 2 patients who developed a fracture for qualitative observation of cyclic axial deformation), and data from an analysis completed by the sponsor on a competitor's infrarenal AAA device using cardiac-gated CT imaging.

FEA was conducted on the transrenal stent with the physiologically-relevant axial compression range. The calculated device strains exceeded the material constant life line at the cranial "x" location regardless of the applied axial deformation magnitude. Moreover, with increased deformation magnitudes, locations pertaining to the cranial tip, caudal "x" and the cranial strut location also begin to show susceptibility to fracture, suggesting that these locations are secondary fracture locations. This analysis predicted that the most likely location of stent fracture is the cranial "x" with the secondary fracture locations being the cranial tip and the caudal "x" location, which is consistent with the observations in the INSPIRATION clinical study. Bench fatigue tests of the transrenal stent under cyclic axial deformations corroborated the cranial "x" location as the primary fracture location under this deformation mode (**Figure 4**). However, the FEA and additional testing did not identify clinical conditions specific to patients with fractures as compared to those without fractures.

As implant migration is a risk of transrenal stent fracture, the sponsor completed acute and chronic migration resistance testing on device test samples that represent the worst-case fracture condition. This chronic testing was conducted in a 37°C saline bath using a 30 mm aortic bifurcate component deployed in a silicone vessel with cyclic loading intended to simulate a 60° neck angulation with an increasing number of induced fractures. Each chronic test with a given number of induced fractures was conducted to 10 million cycles (or 3 months equivalent). Results indicated that migration (i.e.,

movement greater than 10 mm) did not occur with 10 out of the 16 stent struts fractured (i.e., only 3 suprarenal barbs remained intact).

The acute migration resistance testing was conducted in air at 37°C after the 30 mm aortic bifurcate component was deployed into a silicone vessel. The barbs were cut sequentially around the circumference for testing. Results indicated that the aortic bifurcate component did not migrate more than the 10 mm specification until more than 12 stent strut fractures were induced.

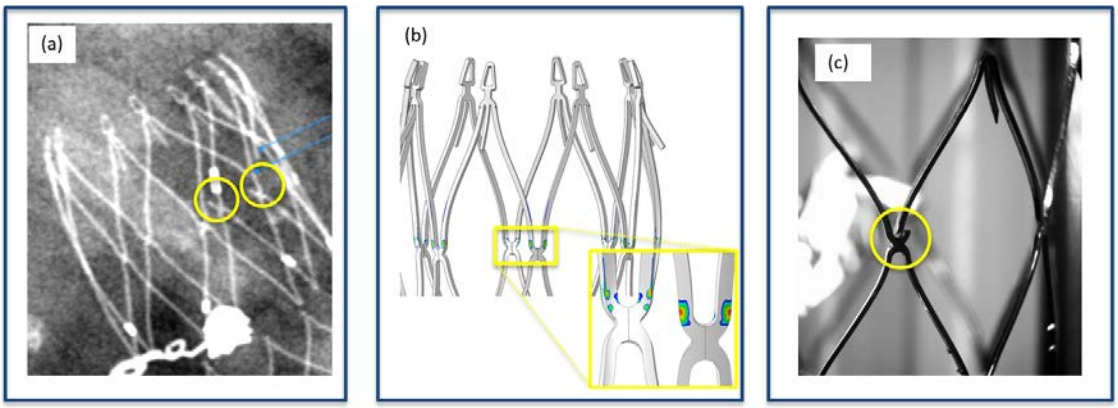


Figure 4. Summarized root-cause of stent strut fractures depicted by (a) primary fracture location in INSPIRATION study; (b) primary fracture location predicted by computational modeling and (c) primary fracture location predicted by bench fatigue testing.

B. Animal Studies

In vivo animal study testing was conducted on the INCRAFT to evaluate the safety of the device following implantation in ovine aorta and iliac arteries. The test article consisted of a 22mm aortic bifurcate prosthesis and a shortened 13mm iliac limb prosthesis. One aortic bifurcate prosthesis was placed transrenally in the aorta and one iliac limb prosthesis was placed separately in the right iliac artery of each animal. The tissue response to INCRAFT was evaluated histologically and the sealing capability and integrity of the bifurcate and iliac limb were evaluated angiographically and radiographically, respectively. Migration was evaluated angiographically. The effect of trans-renal implantation of the aortic bifurcate on renal function was also assessed. Results are presented in **Table 5.** The results demonstrated adequate acute performance, acceptable stent graft integrity and fixation, and appropriate healing characteristics and tissue response.

Table 5: Summary of INCRAFT In-Vivo Studies

Study	# of Animals	Objectives	Results
A 30 Day and 180 Day GLP Safety Study to Evaluate	6 animals in 30-day cohort	To evaluate healing characteristics and tissue response	INCRAFT was interpreted to have appropraite tissue biocompatibility with little to no device related inflammation, rare mural injury, negligible neointima formation, optimal luminal characteristics (e.g.,

Cordis' INCRAFT™ Abdominal Aortic Aneurysm (AAA) Stent Graft System in a Sheep Model	7 animals in 180-day cohort		percent area occlusion) and no device-related mortality.
		To evaluate the sealing capability	Some branches appear to be filling following implant and prior to termination. Due to the implant configuration chosen for this study, which is not representative of the clinical application, it appears these branches are filling due to retrograde flow.
		To evaluate stent graft migration	Angiographic images for this were reviewed and based on the post-implant and pre-termination angiography, no gross migration occurred.
		To evaluate the Stent:Artery Ratio	As expected, Stent to artery ratios were high compared to that target human condition. As a result of the high stent:artery ratio it is likely arteries experienced higher amounts of radial force than one would anticipate in a comparable human case.
		To evaluate the structural integrity of the stent graft	There was no radiographic evidence of strut fractures.
		To evaluate the acute performance by a physician	The implanting physician rated all areas of performance as acceptable and performed well above minimal requirements for acceptable rating.
		To evaluate renal function during the study	No clinical or histological indications of renal impairment.
		To evaluate overall animal health during the study	There was no significant trending noted in the clinical pathology or daily observations and the animals were in good general health over the course of the study with no device-related mortality.

C. Biocompatibility

The biocompatibility assessment performed for the INCRAFT was based on the matrix for body contact and contact duration included in ISO 10993-1:2009/Cor 1:2010, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process. For purposes of biocompatibility testing, the stent graft was classified as an implant device, permanent contact (> 30 days), while the delivery system was classified as an external communicating device, circulating blood, limited exposure (< 24 hours). All testing was performed by a qualified contract laboratory in accordance with FDA GLP Regulations, 21 CFR Part 58.

All testing performed met the pre-specified acceptance criteria. The results are summarized in **Table 6** for the implant and **Table 7** for the delivery system.

Table 6: Biocompatibility Evaluation – INCRAFT Implant

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO MEM Elution Cytotoxicity	To determine if stent graft extracts cause cytotoxicity when exposed to mouse L-929 fibroblast cells	Non-cytotoxic: Grade 0 (no reactivity)	Yes

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO Guinea Pig Maximization Sensitization	To evaluate the allergenic/sensitization potential of stent graft extracts in guinea pigs	Non-sensitizer: All animals scored 0 resulting in 0% sensitization rate	Yes
ISO Intracutaneous Reactivity	To evaluate stent graft extracts for potential irritation effects after intracutaneous injection in rabbits	Non-irritant: All injection sites scored 0	Yes
ISO Acute Systemic Toxicity	To evaluate stent graft extracts for potential toxic effects after single-dose systemic injections in mice	Animals treated with stent graft extracts did not exhibit greater biological response than controls	Yes
Material Mediated Pyrogenicity	To evaluate the stent graft for the potential of inducing a pyrogenic response in rabbits	Non-pyrogenic: rabbits showed a maximum temperature rise of 0.1, 0.2, and 0.2 °C, respectively over the 3 hour test period	Yes
Genotoxicity/ Mutagenicity			
• Ames Assay	To evaluate the mutagenic potential of the stent graft by measuring its ability to induce back mutations at selected loci of several strains of bacteria	Non-mutagenic: The stent graft did not cause an increase in point mutations, exchanges or deletions	Yes
• *In vitro* Mouse Lymphoma	To evaluate the potential of the stent graft extracts to induce a forward mutation in the TK gene of L5178Y TK+/- cells	Non-genotoxic and non-mutagenic: Mutant frequencies and cloning efficiencies of preparations treated with stent graft were within the limits defined for a negative response	Yes
• *In vivo* Mouse Micronucleus	To evaluate the potential of the stent graft to induce micronuclei formation in immature polychromatic erythrocytes (mPCEs) present in the bone marrow of adult CD-1 mice	Non-genotoxic and non-clastogenic: No statistically significant in the number of mPCEs observed with the stent graft	Yes
Hemocompatibility			
• Hemolysis	To evaluate the potential of the stent graft to cause hemolysis in direct contact or by extraction	Non-hemolytic: percent hemolysis: Direct contact – 0.7% Extract – 0.0%	Yes
• Partial Thromboplastin Time (PTT)	To determine the time citrated plasma exposed to stent graft takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride	Non activator of intrinsic coagulation pathway: The stent graft had an average clotting time of 300 seconds (100% of the negative control)	Yes

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
• Platelet and Leukocyte Count	To determine if the stent graft exposed to whole blood would adversely affect the make-up of the platelet and leukocyte components of the blood	Leukocyte counts 93% of control; Platelet counts 106% of control	Yes
• Complement Activation	To measure complement activation in normal human serum (NHS) when serum is exposed to the stent graft	C3a – 0.6% activation compared to cobra venom factor SC5b-9 – 0.0% activation compared to cobra venom factor	Yes
Rabbit Intramuscular Implant (including Chronic Toxicity)			
• 13 week	To evaluate the potential for local and systemic toxic effects of a test article in direct contact with skeletal muscle of the rabbit for 13 weeks	Non-irritant with an irritant ranking score of 0.7; No biologically significant changes to clinical chemistry or hematology	Yes
• 26 week	To evaluate the potential for local and systemic toxic effects of a test article in direct contact with skeletal muscle of the rabbit for 26 weeks	Non-irritant with an irritant ranking score of 1.6; No biologically significant changes to clinical chemistry or hematology	Yes
In vivo Thrombogenicity		N/A*	

***In vivo** thrombogenicity of the implant was assessed in the 30- and 180-day *in vivo* safety studies.

Table 7: Biocompatibility Evaluation – INCRAFT Delivery System

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO MEM Elution Cytoxicity	To determine if delivery system extracts cause cytotoxicity when exposed to mouse L-929 fibroblast cells	Non-cytotoxic: Grade 0 (no reactivity)	Yes
ISO Guinea Pig Maximization Sensitization	To evaluate the allergenic/sensitization potential of delivery system extracts in guinea pigs	Non-sensitizer: All animals scored 0 resulting in 0% sensitization rate	Yes
ISO Intracutaneous Reactivity	To evaluate delivery system extracts for potential irritation effects after intracutaneous injection in rabbits	Non-irritant: the difference between each test extract overall mean score and corresponding control overall mean score was 0.0 and 0.1 for the 0.9% sodium chloride (SC) and sesame oil (SO) test extracts, respectively	Yes

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO Acute Systemic Toxicity	To evaluate delivery system extracts for potential toxic effects after single-dose systemic injections in mice	Animals treated with delivery system extracts showed no mortality or evidence of systemic toxicity	Yes
Material Mediated Pyrogenicity	To evaluate the delivery system for the potential of inducing a pyrogenic response in rabbits	Non-pyrogenic rabbits showed a maximum temperature rise of 0.0, 0.0, and 0.3 °C, respectively over the 3 hour test period	Yes
Genotoxicity/ Mutagenicity			
• Ames Assay	To evaluate the mutagenic potential of the delivery system by measuring its ability to induce back mutations at selected loci of several strains of bacteria	Non-mutagenic: The delivery system did not cause an increase in point mutations, exchanges or deletions	Yes
• *In vitro* Mouse Lymphoma	To evaluate the potential of the delivery system extracts to induce a forward mutation in the TK gene of L5178Y TK+/- cells	Non-genotoxic and non-mutagenic: Delivery system extracts did not cause a two-fold or greater increase in the mean mutant frequency	Yes
• *In vivo* Mouse Micronucleus	To evaluate the potential of the delivery system to induce micronuclei formation in immature polychromatic erythrocytes present in the bone marrow of adult CD-1 mice	Non-genotoxic and non-clastogenic: Extracts of the delivery system did not induce micronuclei formation in mice	Yes
Hemocompatibility			
• Hemolysis	To evaluate the potential of the delivery system to cause hemolysis in direct contact or by extraction	Non-hemolytic: percent hemolysis: Direct contact – 0.5% Extract – 0.0%	Yes
• Partial Thromboplastin Time (PTT)	To determine the time citrated plasma exposed to delivery system takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride	Minimal activator of intrinsic coagulation pathway: The delivery system had an average clotting time of 195.2 seconds (81% of the negative control)	Yes
• Platelet and Leukocyte Count	To determine if the delivery system exposed to whole blood would adversely affect the make-up of the platelet and leukocyte components of the blood	Leukocyte counts 99% of control; Platelet counts 105% of control	Yes

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
• Complement Activation	To measure complement activation in normal human serum (NHS) when serum is exposed to the delivery system	C3a – 4.0% activation compared to cobra venom factor SC5b-9 – 3.6% activation compared to cobra venom factor	Yes
In vivo Thrombogenicity	To evaluate the thrombogenic potential of the delivery system	Minimal thrombus formation (score =1); similar to slightly better thromboresistance than control	Yes

D. Sterilization, Packaging, and Shelf-Life

The INCRAFT is a single-use device that is provided sterile to the end user. The INCRAFT is sterilized using 100% Ethylene Oxide (EO) gas with heated aeration to allow for residual sterilant dissipation. The sterilization process was validated to demonstrate a Sterility Assurance Level (SAL) of 10^{-6}.

All packaging and shelf life validation testing was performed on sterilized dummy devices that had been environmentally conditioned and transportation tested. All protocol acceptance criteria were met, and the results of the testing demonstrated that the packaging configuration for the INCRAFT is capable of maintaining package and sterile integrity for a two (2) year shelf-life.

Specific engineering testing completed to support shelf life are denoted by an asterisk (*) in **Table 4**. Accelerated shelf-life product testing conducted on the INCRAFT supports a 2-year shelf-life claim.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of endovascular repair of infrarenal abdominal aortic aneurysms with the INCRAFT device in the United States (US) and Japan under IDE #G120003. Data from this clinical study were the basis for the PMA approval decision.

Although the primary effectiveness endpoint was at 1 year, at the time of the data lock for PMA submission, complete 4-year data of the INSPIRATION clinical study were available. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between July 2012 and August 2013. The database for this original PMA reflected data collected through December 29, 2017 and included 190

patients (134 in the US and 56 in Japan). There were 32 investigational sites in the United States (27) and Japan (5).

The study was a multi-center, prospective, open label, non-randomized, single arm clinical study. The primary safety endpoint was defined as the proportion of patients with a Major Adverse Event (MAE) within 30 days post index procedure.

H_0: $P_{MAE} \geq 20\%$ vs. H_a: $P_{MAE} < 20\%$

Where, P_{MAE} is the proportion of patients who have at least one MAE at 30 days post-procedure among the INCRAFT patients.

The primary effectiveness endpoint was defined as the propotion of patients with aneurysm treatment success within 1 year post index procedure.

H_0: $P_{Success} \leq 80\%$ vs. H_a: $P_{Success} > 80\%$

Where, $P_{Success}$ is the proportion of patients with successful aneurysm treatment after the use of the INCRAFT through 1 year post-procedure.

The results were tested against a performance goal derived from the open surgical control group in the Society of Vascular Surgery (SVS) Lifeline Registry for the safety endpoint (herein referred to as the SVS Controls) and a performance goal derived from recent IDE studies for EVAR for the effectiveness endpoint.

The hypothesis of the primary safety endpoint was that the 30-day MAE rate in the INCRAFT™ arm was lower than performance goal of 20%. With expected attrition of 5%, a final sample size of 190 patients ensured that 180 evaluable patients were available at 30 days for the primary safety analysis. With a sample size of 180, a one-sided exact binomial test using a nominal significance level of 0.05 had at least 95% power to reject the null hypothesis when the 30-day MAE rate is 10%.

The hypothesis of the primary effectiveness endpoint was that the proportion of patients with the composite endpoint of successful aneurysm treatment was greater than the performance goal of 80%. Assuming a 20% attrition rate over 12 months, the total enrollment was 190 patients. With a sample size of 150, a one-sided exact binomial test using a nominal significance level of 0.05 had approximately 90% power to reject the null hypothesis when the successful aneurysm treatment rate at 12 months was 89%.

The INSPIRATION study utilized external evaluation groups, whose roles and responsibilities are described below:

- *Independent Reviewers:* In order to confirm that only appropriate patients would be enrolled, an independent reviewer reviewed all screening CT imaging to confirm the patients met eligibility criteria prior to enrollment. The

team of independent reviewers were vascular surgeons, separate from the sponsor, Core Laboratory, and sites. Each independent reviewer was trained to the protocol inclusion and exclusion criteria, the INCRAFT device, and the imaging software.

- *Core Laboratory:* A Core Laboratory was utilized to evaluate Angiograms, CT scans, and X-ray images from screening through the 5-year follow-up. They assessed the following events: aneurysm enlargement, endoleaks, stent fracture, and stent graft migration. Two Core Laboraties were used in this pivotal study. The first Core Lab evaluated all images through the first year. The second Core Lab reviewed all imaging after the first year. The second Core Lab re-reviewed all x-rays for the detection of fracture(s) and also re-calculated the 1-month baseline measurements due to changes in migration measurement process from the first Core Lab. The 1-month aneurysm diameter measurements were not re-evalutaed by the second Core Lab as both laboratories used the same definition.

- *Clinical Events Committee:* The Clinical Events Committee (CEC) reviewed and adjudicated protocol-defined MAEs, endograft occlusions, secondary interventions and Type I, III, and IV endoleaks. Type II endoleaks were reviewed by the CEC only if there was a discrepancy between the Site and Core Lab assessment.

- *Data Safety Monitoring Board (DSMB):* The Data Safety Monitoring Board (DSMB) served as an independent group of experts that periodically reviewed and evaluated the accumulated study data for patient safety, study conduct, and study progress.

1. Clinical Inclusion and Exclusion Criteria

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

- Male or Female age 20-years or older;
- Proximal aortic neck is 17-31 mm in diameter;
- Supra-renal aorta, at 20 mm above the anticipated landing location, is smaller than the nominal diameter of the aortic bifurcate prosthesis to be used;
- Infra-renal aortic neck is ≥ 10 mm in length with supra-renal and infra-renal angulations ≤ 60°;
- Subject has at least one of the following:
  - Abdominal aortic aneurysm (AAA) size > 5.0 cm;
  - Increase of the AAA diameter of >0.5 cm over the last 6 months;
- Abdominal treatment length (lowest renal artery origin to aortic bifurcation) ≥ 9.4 cm;
- Aortic bifurcation > 18 mm in diameter;
- Iliac landing zone ≥ 15 mm in length;

- Iliac landing zone 7-22 mm in diameter;
- Minimum access vessel size of $\geq$ 5 mm;
- Minimum overall AAA treatment length (from lowest renal artery to distal landing zone) of 128 mm;
- Women of child bearing potential must be non-pregnant, non-lactating, and not planning to become pregnant during the course of the trial; and have a negative urine or serum pregnancy test within 7 days prior to index procedure;
- Provide written informed consent and as applicable written HIPAA (Health Insurance Portability and Accountability Act) authorization (for U.S. sites only) prior to initiation of study procedures;
- Willing to comply with the specified follow-up evaluation schedule.

Patients were <u>not</u> permitted to enroll in the INSPIRATION study if they met any of the following exclusion criteria:

- Vascular anatomy in which the placement of the stent-graft will cause occlusion of both internal iliac arteries or necessitates surgical occlusion of both internal iliac arteries;
- Subject has one of the following:
  - Aneurysm sac rupture or leaking abdominal aortic aneurysm;
  - Mycotic, dissecting, or inflammatory abdominal aortic aneurysm;
  - Clinically significant acute vascular injury due to trauma;
- Significant aortic or iliac mural thrombus, plaque or calcification that would compromise fixation and seal of the device;
- A conical aortic neck defined as > 3 mm distal increase over a 10 mm length in the planned seal zone;
- Thoracic aortic aneurysm $\geq$ 45 mm;
- Any aortic dissection;
- Morbid obesity (BMI > 40.0 kg/m^2) or other clinical conditions that limit required imaging studies or visualization of the aorta;
- Renal insufficiency (Creatinine >2.0 mg/dL) or subject on renal dialysis;
- Known allergy or intolerance to nickel titanium (nitinol), Polyethylene terephthalate **(**PET), or polytetrafluoroethylene (PTFE);
- Known contraindication to undergoing angiography or anticoagulation (e.g. contrast allergies which cannot be treated);
- Connective tissue disorder (such as Marfan's Syndrome or Ehlers-Danlos Syndrome);
- Coagulopathy, bleeding disorder, or other hypercoagulable state;
- Organ transplant recipient or subject requiring systemic immunosuppressant therapy;
- Cerebral vascular accident (CVA), MI, or intracranial bleeding within 3 months prior to the procedure;
- Active infection or chronic systemic illness at the time of index procedure that may interfere with the study objectives;

- Major surgical procedure within 1 month prior to the index procedure or pre-planned within 1 month afterwards;
- Co-existing condition with a life expectancy of less than 2-years at time of procedure;
- Current or planned participation in any other investigational drug or medical device clinical study that has not completed primary endpoint(s) evaluation;
- Existing AAA surgical graft and/or a AAA stent-graft system;
- Other medical, social, or psychological issues that in the opinion of the investigator preclude the subjects from receiving this treatment, and the procedures and evaluations pre- and post-treatment.

2. Follow-up Schedule

All patients were scheduled to return for follow-up visits at the investigational site at 1 month, 6 months, 1 year post-procedure and annually through 5 years. A subset of patients (i.e., those with at least one fracture identified within the first 5 years) will be followed for an additional 5 years, for a total of 10 years post index procedure.

Pre-operative assessment included medical history, physical exam, CT scan, patient-reported outcomes questionnaire and laboratory testing as well as a pregnancy test for female patients of childbearing potential.

Post-operatively, the objective parameters measured during the study included clinical utility measures (e.g., post index procedural length of hospital stay (days) and length of Intensive Care Unit (ICU) stay (hours)), acute procedural information, appropriate effectiveness measures, and concomitant medications, with physical examination, CT scans with and without contrast, four-plane X-rays, and patient-reported outcomes questionnaires.

Pre-operative and post-operative parameters measured during the study are described in the Time and Event Schedule, **Table 8**.

Adverse events and complications were recorded at all visits.

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

Table 8: Time and Event Schedule

	Screening	Index	Discharge Assessments	1 month +/- 7 days	6 months +/- 30 days	1 year +/- 30 days	2 – 5 years[9]
Informed Consent	X[1]						
Medical History	X[1]						
Physical examination	X[1]		X	X	X	X	X
Verify Inclusion / Exclusion Criteria	X[1]	X					
Labs: complete blood count (CBC), serum creatinine	X[2]						
Angiogram		X					
CT scan w/ & w/o contrast	X[3]			X[4]	X[4]	X[4]	X[4]
X-ray (abdominal)				X[5]	X[5]	X[5]	X[5]
Adverse Event assessment		X	X	X	X	X	X
Patient-Reported Outcomes (PRO) Questionnaire SF36v2	X[6]			X[6]	X[6]	X[6]	
Conc. Medication at time of visit	X	X[7]	X	X	X	X	X

1 Month = 30 Days 1 Year = 360 Days[8]

[1] Prior to any study related procedure and within 6 weeks prior to index procedure

[2] Labs must be within 6 weeks prior to index procedure

[3] CT Reconstructions, a CT-scan (with contrast) performed within 6 months before index procedure is accepted. Screening CT-scan (w/o contrast) is optional and should be submitted to the independent Core Lab.

[4] For subjects who develop renal insufficiency after index procedure, a duplex ultrasound (DUS) can replace the contrast CT (CT without contrast remains mandatory)

[5] X-rays are required for all four abdominal views (AP, lateral, and 2 oblique views)

[6] The SF36v2 PRO questionnaire must be fully completed by the patient prior to receipt of clinical assessments, tests, or study related procedures and can also be fully administered over the phone in the event a patient cannot return for their follow-up visit

[7] Medication given to the subject at the time of index procedure

[8] This timing convention is used throughout the protocol

[9] 2 years +/-45 days, 3 years +/-60 days, 4 years +/-75 days and 5 years +/-90 days

3. Clinical Endpoints

With regards to safety, the primary safety endpoint was the incidence of major adverse events (MAEs) at 30 days post-procedure. A major adverse event was defined as any of the following:

- Death
- Stroke
- Myocardial infarction
- New onset renal failure (requiring dialysis)
- Respiratory Failure (requiring mechanical ventilation)
- Paralysis/ paraparesis
- Bowel Ischemia (requiring surgical intervention)
- Procedural Blood Loss (≥ 1,000 cc)

This primary safety endpoint was compared to a performance goal of 20%.

With regards to effectiveness, the primary effectiveness endpoint was successful aneurysm treatment, which was a composite endpoint defined as the following.

- Technical success at the conclusion of the index procedure, that is, successful insertion of the delivery system through the vasculature and successful deployment of the device at the intended location. The endovascular graft must be patent, with absence of Types I or III endoleaks or aneurysm sac rupture, at the time of procedure completion as confirmed by angiography or other imaging modality;
- Absence of postoperative aneurysm enlargement (growth > 5 mm), or stent graft migration (> 10 mm), as compared to the 1 month size measurement at any time up to 1 year; and
- Absence of postoperative conversion to open surgery, aneurysm sac rupture, endoleak Type I/ III, or graft occlusion (including unilateral or bilateral limb occlusion) at any time up to 1 year.

This primary effectiveness endpoint was compared to a performance goal of 80%.

With regard to success criteria, the study would be considered successful if the performance goal for the safety and effectiveness primary endpoints were met.

The following secondary analyses were performed using descriptive summary statistics:

- Secondary safety endpoints include the following:
  - Major Adverse Events (MAEs) and the individual components at 180 days and 360 days compared with SVS Open Surgical Controls, wherever the appropriate control data is available. These endpoints will be reported annually to 5 years;
  - Procedure-related complications through 30 days, 180 days, 360 days and annually to 5 years;

- Secondary effectiveness endpoints include the following:
  - Aneurysm-related mortality at 30 days, 180 days, 360 days, and annually through 5 years;
  - Technical Success at 30 days as confirmed by CT or other imaging modality;
  - Clinical utility measures to be compared with SVS Open Surgical Controls include:
    - Length of hospital stay (days) post index procedure;
    - Length of Intensive Care Unit (ICU) stay (hours) post index procedure;
    - Length of the Index procedure (minutes).
  - Incidence of secondary interventions, or the need for secondary interventions, to repair vascular events or malfunctions which are related to

device and/or peri-graft complications at 1 month, 6 months, 1 year and annually to 5 years. Secondary intervention is any vascular event which requires intervention to repair the AAA or device, Indications for secondary intervention may include endoleaks, stent graft migration, occlusion, or aneurysm sac rupture.

- The incidence of secondary interventions within 1 year post-procedure, needed to prevent the occurrence of a significant event. Significant event being defined as: aneurysm enlargement (growth > 5 mm), stent graft migration (> 10 mm) compared to the 1-month size, endoleak type I / III, graft occlusion, sac rupture.
- Device-related events at 1 month, 6 months, 1 year and annually to 5 years. The device-related event may include:
  - Aneurysm Enlargement – defined as an increase in maximum aneurysm cross sectional diameter > 5 mm compared to the 1 month measurement;
  - Endoleak(s);
  - Aneurysm sac rupture;
  - Fracture(s);
  - Delivery System Malfunction;
  - Device Malfunction;
  - Stent Graft Migration – evidence of proximal or distal movement of the stent graft >10 mm relative to fixed anatomic landmarks compared with 1 month;
  - Graft Occlusion (including unilateral or bilateral limb occlusion);
  - Conversion to open surgery.

B. Accountability of PMA Cohort

At the time of database lock, of 190 patients enrolled in the PMA study, 100% of patients were available for analysis of the primary safety endpoint at 1 month and 96.3% (183) were available for analysis of the primary effectiveness endpoint at 1 year.

One hundred and ninety patients (190) were implanted with the INCRAFT® AAA Stent Graft System and seen through discharge. Ninety nine percent (99%) of the eligible patients (189/190) completed the 1 month follow-up visit. One patient died 2-days post-operatively. The visit compliance rate was 97% (182/188) at 6 months and 97% (177/183) at 1 year. There was at least 90% imaging compliance up to the 1 year visit with suitability for evaluating endoleaks, aneurysm enlargement, migration, and stent fracture. There were two (2) conversions to open surgery after the 6 month visit but prior to the 1 year visit and the devices were explanted in each case. The patients who underwent conversion did not have follow up imaging post-conversion as the INCRAFT device was no longer present; however, they continue annual clinical follow up. One patient who underwent an axillo-bifemoral bypass procedure to address a patency event at the 4 year timepoint (Stent Graft Patency **Section 2.2.9**) is continuing to be followed via clinical and imaging follow-up for endovascular graft

assessment. Beyond the 1-year visit, there was at least 85% imaging compliance at 2 years, at least 82% imaging compliance at 3 years, and at least 70% imaging compliance at 4 years, with suitability for evaluating endoleaks, aneurysm enlargement, migration, and stent fracture. Detailed patient accountability and follow-up are presented in **Table 9**.

Table 9. Patient Imaging Accountability

		Number of Patients (%)				Adequate Imaging to Assess the Parameter[6] # (%) (Core Lab data)				Events Occurring before Next Interval # (%)			
Visit	**Eligible[1]**	**Clinical data[2]**	**CT[3]**	**KUB XRAY[4]**	**FU pending[5]**	**Endoleak**	**Aneurysm Expansion**	**Migration**	**Fracture**	**Conversion[7]**	**Death[8]**	**LTF[9]**	**Not due for visit[10]**
Procedure	190	190	N/A	N/A	0	190/190 (100%)[11]	N/A	N/A	N/A	0	0	0	0
Discharge	190	190	N/A	N/A	0	190/190 (100%)[12]	N/A	N/A	N/A	0	0	0	0
1 Month	190/190[13] (100%)	189/190 (99%)	188/190 (99%)	183/190 (96%)	0	186/190 (98%)	188/190 (99%)	187/190 (98%)	183/190 (96%)	0	2/190 (1%)	0	0
6 Months	188/190 (99%)	182/188 (97%)	178/188 (95%)	173/188 (92%)	0	175/188 (93%)	176/188 (94%)	177/188 (94%)	172/188 (91%)	2/188 (1%)	2/188 (1%)	3/188 (2%)	0
1 Year	183/190 (96%)	177/183 (97%)	173/181 (96%)	164/181 (91%)	0	167/181 (92%)	173/181 (96%)	172/181 (95%)	163/181 (90%)	0	6/183 (3%)	5/183 (3%)	0
2 Years	172/190 (91%)	162/172 (94%)	155/170 (91%)	144/170 (85%)	0	149/170 (88%)	155/170 (91%)	154/170 (91%)	144/170 (85%)	0	6/172 (3%)	5/172 (3%)	0
3 Years	161/190 (85%)	148/161 (92%)	142/159 (89%)	132/159 (83%)	0	131/159 (82%)	142/159 (89%)	141/159 (89%)	132/159 (83%)	0	10/161 (6%)	3/161 (2%)	0
4 Years	148/190 (78%)	129/148 (87%)	113/146 (77%)	108/146 (74%)	0	102/146 (70%)	112/146 (77%)	112/146 (77%)	108/146 (74%)	0	11/148 (7%)	5/148 (3%)	0

Visit windows are defined based on imaging windows:
Procedure (day 0), Discharge (1- discharge), 1 Month (discharge - 90 days), 6 Months (91 - 270 days), 1 Year (271 - 540 days), 2 Years (541 - 900 days), 3 Years (901 - 1260 days), 4 Years (1261 - 1620 days), and 5 Years (1621 - 1980 days).

[1]Eligible for follow-up = (previous eligible for follow-up – previous death - previous LTF) – currently not due). Patient(s) not due for a visit are excluded from the denominator.

[2]Defined as patients with either the scheduled study visit or patients with an unscheduled study visit within the imaging window for the visit.

[3]Only images that pass QC are listed.

[4]Only images that pass QC are listed.

[5]Patients still within follow-up window but have not had clinical follow up.

[6]Not the number of subjects with these reported events, but rather, the number with adequate imaging to evaluate the listed outcome.

[7]Patients who converted to open surgery no longer completed imaging follow-up, only clinical follow-up.

[8]Deaths within imaging windows.

[9]Lost to Follow-up (LTF) are those subjects that are either withdrawn or classified as lost to follow-up in the Electronic Data Capture.

[10]Number of patients who are still alive and participating in the study but have not had the device implanted long enough to be eligible for the follow-up visit. Percent of patients is out of those who are still alive (not dead) and participating in the study (not LTF).

[11]Endoleak at procedure determined by angiogram. Adequate imaging count provided by sponsor, angiogram Core Lab data not received by Contract Research Organization (CRO).

[12]Endoleak at discharge determined by CT. Adequate imaging count provided by sponsor, CT at discharge Core Lab data not received by CRO.

[13]The denominator for eligibility at 1 month is based on the 1 month imaging window defined as "post-procedure through 90 days." The 2 patients died at 2 days and 78 days within the 1 month imaging window therefore they were included in the denominator.

C. Study Population Demographics and Baseline Parameters

Demographics

The demographics of the study population are typical for a pivotal study performed in the US for the evaluation of an endovascular graft system intended for infrarenal abdominal aortic aneurysm repair, with the exception of a higher percentage of non-white/Caucasian study patients.

Patient demographics for the INCRAFT cohort and SVS controls are presented in **Table 10**. The INCRAFT cohort was older (73.8 years vs. 70.1 years SVS) and shorter in stature (172 cm vs. 174 cm SVS) than the SVS controls. In addition, the INCRAFT cohort included more males (90% vs. 83.3% SVS). The INCRAFT cohort was only 68.9% white/Caucasian as compared with the SVS controls (94.9%) because roughly one-third of the patients in the INCRAFT cohort were from Japan while all the patients in SVS controls were from the US.

The patients in the US cohort were slightly older (74.5 vs. 72.1 years) and taller (174.8 vs. 165.8) with a higher body mass index (28.6 vs. 24.6) as compared to the Japanese cohort. The percentage of women enrolled in the study was higher in the US (13.4%) as compared to Japan (1.8%).

Table 10. Patient Demographics

Patient Characteristics	INCRAFT US (N = 134)	INCRAFT Japan (N = 56)	INCRAFT US & Japan (N = 190)	SVS Controls (N = 323)
Age (years)				
Mean ± SD (N)	74.5 ± 7.48 (134)	72.1 ± 7.55 (56)	73.8 ± 7.56 (190)	70.1 ± 7.41 (323)
Median	75.0	71.0	74.0	70.7
Range (Min, Max)	51.0, 89.0	56.0, 90.0	51.0, 90.0	41.2, 86.1
Number of Men (%)	86.6% (116/134)	98.2% (55/56)	90.0% (171/190)	83.3% (269/323)
Height (cm)				
Mean ± SD (N)	174.8 ± 8.96 (134)	165.8 ± 7.09 (56)	172.1 ± 9.37 (190)	174.0 ± 9.26 (315)
Median	177.8	166.0	172.7	175.3
Range (Min, Max)	150.0, 196.0	147.0, 179.5	147.0, 196.0	135.0, 194.3
Weight (kg)				
Mean ± SD (N)	87.6 ± 15.78 (134)	67.7 ± 11.87 (56)	81.7 ± 17.27 (190)	82.9 ± 17.25 (318)
Median	86.2	69.9	80.5	83.0
Range (Min, Max)	48.6, 137.8	35.9, 96.2	35.9, 137.8	40.4, 151.5

Patient Characteristics	INCRAFT US (N = 134)	INCRAFT Japan (N = 56)	INCRAFT US & Japan (N = 190)	SVS Controls (N = 323)
BMI (kg/m^2)				
Mean ± SD (N)	28.6 ± 4.49 (134)	24.6 ± 3.74 (56)	27.4 ± 4.66 (190)	27.3 ± 5.07 (314)
Median	27.9	24.9	27.1	27.1
Range (Min, Max)	19.7, 40.0	15.1, 34.4	15.1, 40.0	15.8, 63.1
Race				
White/Caucasian	97.8% (131/134)	0.0% (0/56)	68.9% (131/190)	94.9% (244/257)
Non-White/Non-Caucasian	2.2% (3/134)	100.0% (56/56)	31.1% (59/190)	5.1% (13/257)

Baseline Medical History

Baseline clinical history for the study patients is summarized in **Table 11** according to body system and/or medical condition. The cardiovascular comorbidities that were most commonly observed in the INCRAFT cohort were hypertension (77.9%) and hypercholesterolemia (72.1%).

A larger proportion of patients in the SVS controls had angina (25.5% vs. 15.8%), coronary artery disease (53.3% vs. 40.5%), history of myocardial infarction (32.8% vs. 18.4%), and stroke (13.6% vs. 6.3%). In contrast, a larger proportion of patients in the INCRAFT cohort had diabetes (25.3% vs. 12.7%), and history of cancer (32.6% vs. 23.6%). There was a high prevalence of smoking history in the INCRAFT cohort (92.6%) and the SVS controls (88.2%).

There were differences between the US patient population and the Japanese patient population with respect to their baseline medical histories as summarized in **Table 11**. The most commonly observed comorbidities were the same in the US and Japan; however, the rates were only similar for hypertension (78.4% vs. 76.8%) and were different for hypercholesterolemia (78.4% vs. 57.1%). The rates of comorbidities at baseline were higher in the US patient population as compared to the Japanese patient population, with the exception of angina (9.0% vs. 32.1%), liver disease (4.5% vs. 8.9%), and percutaneous transluminal coronary angioplasty or stent (22.4% vs. 30.4%).

Table 11. Baseline Medical History

Body System/Medical Condition	INCRAFT US (N = 134)	INCRAFT Japan (N = 56)	INCRAFT US & Japan (N = 190)	SVS Controls (N = 323)
Cardiovascular				
Number of Patients with at least one cardiovascular comorbidity	97.0% (130/134)	87.5% (49/56)	94.2% (179/190)	92.6% (287/310)*
Angina	9.0% (12/134)	32.1% (18/56)	15.8% (30/190)	25.5% (54/212)
Arrhythmia	21.6% (29/134)	10.7% (6/56)	18.4% (35/190)	13.9% (45/323)

Body System/Medical Condition	INCRAFT US (N = 134)	INCRAFT Japan (N = 56)	INCRAFT US & Japan (N = 190)	SVS Controls (N = 323)
Coronary Artery Disease	47.8% (64/134)	23.2% (13/56)	40.5% (77/190)	53.3% (172/323)
Myocardial Infarction	20.1% (27/134)	14.3% (8/56)	18.4% (35/190)	32.8% (106/323)
Hypertension	78.4% (105/134)	76.8% (43/56)	77.9% (148/190)	70.6% (228/323)
Hypercholesterolemia	78.4% (105/134)	57.1% (32/56)	72.1% (137/190)	NA
Congestive Heart Failure	3.7% (5/134)	0.0% (0/56)	2.6% (5/190)	6.5% (21/323)
Family History of Aneurysm	14.2% (19/134)	5.4% (3/56)	11.6% (22/190)	17.9% (38/212)
Peripheral Arterial Disease	18.7% (25/134)	5.4% (3/56)	14.7% (28/190)	18.0% (58/323)
Neurological				
Stroke	6.7% (9/134)	5.4% (3/56)	6.3% (12/190)	13.6% (44/323)
Endocrine				
Diabetes	26.9% (36/134)	21.4% (12/56)	25.3% (48/190)	12.7% (41/323)
Urinary				
Moderate Renal Insufficiency	6.7% (9/134)	1.8% (1/56)	5.3% (10/190)	3.1% (10/323)
Pulmonary				
Chronic Obstructive Pulmonary Disease	30.6% (41/134)	17.9% (10/56)	26.8% (51/190)	26.9% (87/323)
Other Medical Conditions				
Liver Disease	4.5% (6/134)	8.9% (5/56)	5.8% (11/190)	3.4% (5/146)
Cancer	37.3% (50/134)	21.4% (12/56)	32.6% (62/190)	23.6% (50/212)
Alcoholism	11.2% (15/134)	1.8% (1/56)	8.4% (16/190)	8.5% (18/212)
Smoking	91.0% (122/134)	96.4% (54/56)	92.6% (176/190)	88.2% (285/323)

* There were 13 patients who reported no other cardiovascular (CV) comorbidities but missing data for a prior history of angina or a family history of aneurysm for these patients, therefore, they were not included in the denominator.

Baseline Vessel Measurements

Baseline aneurysm and anatomical measurements, as well as access vessel characteristics of the study population, were reported by both the Core Lab and site. Two CT scans were not evaluated by the Core Lab due to imaging quality. Baseline aneurysm characteristics are summarized in **Table 12**.

All patients enrolled in this study met the inclusion criteria based on site-reported CT measurements. Based upon a retrospective review of baseline imaging by the Core Lab, 72.9% (137 patients) were considered to have challenging anatomy, defined by access diameter, stenotic segments, calcification, and tortuosity.

There were no clinically meaningful differences between the patients in the US and Japan with respect to the baseline aneurysm and anatomical measurements.

Table 12. Baseline Vessel Characteristics as Measured from CT Scan

	INCRAFT (All Patients)	
Measure	**Core Lab N = 188†**	**Site Reported N = 190**
Supra-renal Aortic Diameter (mm)		
Mean ± SD (N)	23.6 ± 2.50 (188)	23.9 ± 2.56 (189)
Median	23.50	24.00
Range (min, max)	18.00, 31.50	17.00, 30.00
Aortic Neck Diameter at start of cranial Attachment (mm)		
Mean ± SD (N)	21.7 ± 2.68 (188)	22.6 ± 2.70 (190)
Median	22.00	23.00
Range (min, max)	15.50, 30.00	17.00, 31.00
Aortic neck Constant Reference Diameter at 10 mm inferior (mm)		
Mean ± SD (N)	22.2 ± 3.81 (188)	22.6 ± 3.03 (190)
Median	22.00	22.50
Range (min, max)	16.00, 50.00	16.00, 32.00
Maximum aortic aneurysm Sac Diameter (mm)		
Mean ± SD (N)	54.9 ± 6.90 (188)	55.7 ± 6.58 (190)
Median	53.95	54.00
Range (min, max)	43.30, 98.30	45.00, 100.00
Aortic Diameter at Bifurcation (mm)		
Mean ± SD (N)	19.3 ± 5.50 (188)	25.2 ± 6.56 (190)
Median	18.00	23.00
Range (min, max)	11.00, 48.50	18.00, 52.00
Right caudal landing zone Diameter (mm)		
Mean ± SD (N)	13.8 ± 3.15 (188)	13.5 ± 3.36 (190)
Median	13.20	13.00
Range (min, max)	7.50, 27.00	7.00, 22.00
Left caudal landing zone Diameter (mm)		
Mean ± SD (N)	13.7 ± 2.91 (188)	13.0 ± 3.01 (190)
Median	13.15	13.00
Range (min, max)	8.00, 24.00	7.00, 21.00
Right minimum vessel diameter (mm)		
Mean ± SD (N)	6.8 ± 1.53 (187)	8.1 ± 1.86 (190)
Median	7.00	8.00
Range (min, max)	2.80, 11.10	5.00, 17.00
Left minimum vessel diameter (mm)		
Mean ± SD (N)	6.9 ± 1.50 (187)	8.1 ± 1.82 (190)
Median	7.10	8.00
Range (min, max)	3.30, 11.70	5.00, 14.00

† Two of the 190 CTs received by the Core Lab were deemed as not evaluable due to quality of the imaging.

The distribution of baseline aneurysm diameters is presented in **Table 13**. All patients enrolled in this study met the inclusion criteria based on site-reported CT measurements. As noted in **Table 13**, there were differences observed in the measurements for maximum aneurysm sac diameter between the Core Lab and the sites. This variance between the Core Lab and the site measurements are due to differences in methodology when measuring aneurysm sac diameter.

Table 13. Distribution of Baseline Aneurysm Diameters

	INCRAFT (All Patients)	
Measure	**Core Lab N = 188**†	**Site Reported N = 190**
Maximum aneurysm Sac Diameter (%)		
< 30 mm	0% (0/188)	0% (0/190)
30-39 mm	0% (0/188)	0% (0/190)
40-49 mm	20.2% (38/188)	3.2% (6/190)
50-59 mm	63.8% (120/188)	76.8% (146/190)
60-69 mm	13.3% (25/188)	16.3% (31/190)
70-79 mm	1.6% (3/188)	2.1% (4/190)
80-89 mm	0.5% (1/188)	1.1% (2/190)
≥ 90 mm	0.5% (1/188)	0.5% (1/190)
Aneurysm Diameter < 50 mm (%)	20.2% (38/188)	3.2% (6/190)
Aneurysm Diameter ≥ 50 mm (%)	79.8% (150/188)	96.8% (184/190)
† Two of the 190 CTs received by the Core Lab were deemed as not evaluable due to quality of the imaging.		

INCRAFT Devices Implanted

The number and diameters of the INCRAFT study device components implanted are summarized in **Table 14.** The aortic bifurcate, ipsilateral limb and contralateral limb prostheses were implanted in all patients. The most common aortic bifurcate diameters were 26 and 30 mm and the most common limb diameters were 13, 16 and 20 mm. Iliac limb extensions were used when additional extension was required. The ipsilateral limb extension was implanted in 10 (5.3%) patients while the contralateral limb extension was implanted in 9 (4.7%) patients. Two patients (2/190; 1%) were implanted with both an ipsilateral and a contralateral limb extension.

Table 14: INCRAFT Prothesis Systems Implanted

Prothesis System	Outer Diameter (mm)	Overall (N=190)
Aortic Bifurcate		190 (100%)
	22	15 (7.9%))
	26	85 (44.7%))
	30	71 (37.4%))
	34	19 (10.0%))
Ipsilateral Limb		190 (100%)
	10	3 (1.6%)
	13	34 (17.9%)
	16	78 (41.1%)
	20	53 (27.9%)
	24	22 (11.6%)
Contralateral Limb		190 (100%)
	10	11 (5.8%)
	13	39 (20.5%)
	16	75 (39.5%)
	20	50 (26.3%)
	24	15 (7.9%)
Ipsilateral Limb Extension		10 (5.3%)
	13	4 (2.1%)
	16	1 (0.5%)
	20	2 (1.1%)
	24	3 (1.6%)
Contralateral Limb Extension		9 (4.7%)
	10	2 (1.1%)
	13	2 (1.1%)
	16	1 (0.5%)
	24	4 (2.1%)

Accessory Device Usage

The type and number of accessory devices implanted in the treatment area during the index procedure are summarized in **Table 15**. An aortic extension/cuff was used in 6 patients in Japan to treat a Type IV endoleak in 1 patient, to treat a Type Ib endoleak in 1 patient, and to minimize the risk of future endoleaks in 4 patients. The bare metal stent was placed to treat a tear in the superior mesenteric artery (SMA) caused by the use of a pull-down maneuver to reposition the stent graft which was inadvertently deployed above the renal arteries.

Table 15: Non-Cordis Study Devices Used

Device	Overall (N=190)
Aortic Extension/Cuff	3.2% (6/190)
Post-dilation Balloon	21.6% (41/190)
Balloon Expandable, Bare Metal Stent	0.5% (1/190)

Procedural Data

Table 16 provides the acute procedural data for the INCRAFT cohort including a breakdown of the data for patients treated in the US vs. Japan. The mean duration of the procedure in the INCRAFT cohort was 102.7 minutes, a mean of 97 minutes for patients treated in the US and a mean of 116 minutes for patients treated in Japan. The mean time required to deploy the INCRAFT device (i.e., time from entry of delivery system to final imaging) was 47.5 minutes, which was similar in both the US (48 minutes) and Japan (46 minutes). However, operators (study investigators) in Japan reported a higher fluoroscopy time and contrast volume compared to the operators (study investigators) in the US (30 minutes vs. 23 minutes, and 136 mL vs. 124 mL, respectively). Procedural estimated blood loss of ≥1000 mL was reported in 4 US patients (2.1%) in the INCRAFT cohort, while no estimated blood loss of ≥1000 mL was reported for the Japanese patients. Procedural blood loss of <500 mL among the patients treated in Japan was 98.2% (55/56), while in the US it was 92.5% (124/134). While the estimated blood loss was different between the US and Japan, the transfusion rates were similar (5.2% in US vs. 5.4% in Japan). A total of 3 Japanese patients received a transfusion prophylactically due to advanced age and additionally due to presence of pre-procedure anemia (2 patients). The main differences between the procedural data for US and Japan is related to patients receiving general anesthesia, time in the ICU, and in overall length of hospital stay. A higher proportion of patients (60%, 81/134) treated in the US received general anesthesia compared to those that were treated in Japan (34%, 19/56).

Table 16. Acute Procedural Characteristics – U.S. and Japan

	INCRAFT Patients		
Acute Procedural Data	**Total (N = 190)**	**US (N = 134)**	**Japan (N = 56)**
Duration of Procedure (minutes)			
Mean ± SD (N)	102.7 ± 42.85 (190)	97.0 ± 41.44 (134)	116.4 ± 43.41 (56)
Median	95.5	86.5	115.0
Range (min, max)	30.0, 218.0	30.0, 211.0	44.0, 218.0
Duration of anesthesia (minutes)			
Mean ± SD (N)	179.2 ± 52.85 (99)	176.6 ± 56.46 (80)	190.5 ± 32.47 (19)
Median	169.0	163.0	195.0
Range (min, max)	47.0, 363.0	47.0, 363.0	130.0, 233.0
Total INCRAFT time (minutes)			
Mean ± SD (N)	47.5 ± 22.43 (189)	48.0 ± 22.88 (133)	46.2 ± 21.47 (56)
Median	45.0	45.0	44.5
Range (min, max)	15.0, 165.0	15.0, 165.0	17.0, 124.0
Patients receiving general anesthesia (%)	52.6% (100/190)	60.4% (81/134)	33.9% (19/56)
Volume of contrast used (mL)			
Mean ± SD (N)	127.6 ± 52.24 (189)	124.0 ± 54.72 (133)	136.2 ± 45.12 (56)
Median	122.0	120.0	135.0
Range (min, max)	13.0, 300.0	13.0, 300.0	50.0, 240.0

	INCRAFT Patients		
Acute Procedural Data	**Total (N = 190)**	**US (N = 134)**	**Japan (N = 56)**
Total Fluoroscopy Time (minutes)			
Mean ± SD (N)	25.0 ± 13.48 (190)	22.7 ± 12.60 (134)	30.4 ± 14.11 (56)
Median	21.0	20.0	26.5
Range (min, max)	7.0, 92.0	7.0, 92.0	13.0, 84.0
Estimated blood loss (procedural)			
<500 mL	94.2% (179/190)	92.5% (124/134)	98.2% (55/56)
500-999 mL	3.7% (7/190)	4.5% (6/134)	1.8% (1/56)
≥1000 mL	2.1% (4/190)	3.0% (4/134)	0%(0/56)
Patients requiring blood transfusion during procedure (%)	2.6% (5/190)	3.0% (4/134)	1.8% (1/56)
Patients requiring blood transfusion after procedure (%)	2.6% (5/190)	2.2% (3/134)	3.6% (2/56)
Time in ICU (hours)			
Mean ± SD (N)	8.0 ± 10.59 (184)	4.8 ± 9.56 (128)	15.2 ± 9.25 (56)
Median	0.0	0.0	20.0
Range (min, max)	0.0, 48.0	0.0, 48.0	0.0, 25.0
Overall length of hospital stay (days)			
Mean ± SD (N)	2.7 ± 2.88 (190)	1.5 ± 1.12 (134)	5.6 ± 3.71 (56)
Median	1.5	1.0	4.0
Range (min, max)	1.0, 17.0	1.0, 8.0	2.0, 17.0

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the pivotal study cohort of 190 patients available for the 30-day evaluation. The key safety outcomes for this study are presented below in **Table 17**. Adverse effects are reported in **Table 18, Table 19** and **Table 20**.

1.1. Primary Safety Endpoint

The primary safety endpoint of the specified analysis for the INCRAFT patients met the pre-defined performance goal of 20%. The primary safety results are presented in **Table 17**. The composite 30-day MAE rate was 3.2% (6/190). There was 1 patient that had a myocardial infarction (MI) on post-operative day 2, which resulted in death. There was 1 patient that experienced a stroke (right occipital intraparenchymal hematoma) on post-operative day 16. The Clinical Events Committee adjudicated the event as unlikely related to the index procedure. Addtionally, 4 patients experienced procedural blood loss greater than 1,000 mL. There were no incidences of renal failure, respiratory failure, paralysis/ paraparesis, or bowel ischemia reported.

The primary safety analysis was based on the INCRAFT cohort of 190 patients (i.e., all patients who had the aortic bifurcate device introduced into the body). Patients who experienced at least 1 MAE through 30 days were included in the primary safety analysis even if the patient had not completed a 1-month follow-up visit.

Table 17. Primary Safety Endpoint Results

	INCRAFT**	
Primary Endpoint	**Total Patients (N = 190)**	**95% CI**
Primary Composite Safety Endpoint*	3.2% (6/190)£	(- , 6.1%)
MAE Component Rate at 30 days		
Death†	0.5% (1/190)	
Stroke	0.5% (1/190)	
Myocardial Infarction†	0.5% (1/190)	
New Onset Renal Failure (requiring dialysis)	0% (0/190)	
Respiratory Failure (requiring mechanical ventilation)	0% (0/190)	
Paralysis /Paraparesis	0% (0/190)	
Bowel ischemia (requiring surgical intervention)	0% (0/190)	
Procedural blood loss (≥ 1,000 cc)	2.1% (4/190)	

£ The primary safety endpoint is the proportion of patients with at least 1 MAE through 30 days post-procedure (numerator) over the number of patients with an MAE plus the number of patients without an MAE and with at least 23 days of post-procedure follow-up (denominator).

* Primary Composite Safety Endpoint includes all of the eight individual components listed in this table.

** INCRAFT analysis set includes all patients who had the aortic bifurcate device introduced into the body.

† A patient may report multiple MAEs; hence, number of patients with any MAE may not be the sum of those in each MAE category. One patient experienced both a myocardial infarction and death.

1.2. Secondary Safety Endpoints

1.2.1. Major Adverse Events

Secondary safety endpoints include MAE and the individual components at 6 months and annually through 5 years; and procedure-related complications, defined as complications not attributed to the device but attributed to the procedure which arise following the procedure (e.g., renal insufficiency), through 30 days, 6 months, and annually to 5 years. The overall rate of MAE and the components of MAE post-procedure observed in the clinical study are provided in **Table 18**. The overall rate of MAEs is 7.0% at 6 months, 10.9% at 1 year, 18.8% at 2 years, 22.8% at 3 years and 30.3% at 4 years. The overall MAE rates are primarily driven by the incidence of death, stroke, and myocardial infarction, all deemed unrelated to the INCRAFT by the Clinical Events Committee (CEC).

Table 18. MAE Rate through 4 Years - Overall Rate and MAE Components

Major Adverse Events *	INCRAFT Patients (N = 190)				
	6 Month	1 Year	2 Years	3 Years	4 Years
MAE rate **	7.0% (13/187)	10.9% (20/183)	18.8% (33/176)	22.8% (39/171)	30.3% (50/165)
Death	1.6% (3/187)	3.3% (6/183)	8.0% (14/176)	12.9% (22/171)	21.2% (35/165)
Stroke	1.6% (3/187)	2.2% (4/183)	5.1% (9/176)	7.6% (13/171)	9.1% (15/165)
Myocardial infarction	1.6% (3/187)	3.3% (6/183)	4.0% (7/176)	5.3% (9/171)	7.3% (12/165)
New onset renal failure (requiring dialysis)	0.0% (0/187)	0.0% (0/183)	0.0% (0/176)	0.0% (0/171)	0.0% (0/165)
Respiratory failure (requiring mechanical ventilation)	0.5% (1/187)	1.1% (2/183)	1.1% (2/176)	1.2% (2/171)	1.2% (2/165)
Paralysis / paraparesis	0.0% (0/187)	0.0% (0/183)	0.0% (0/176)	0.0% (0/171)	0.0% (0/165)
Bowel ischemia (requiring surgical intervention)	0.0% (0/187)	0.0% (0/183)	0.0% (0/176)	0.0% (0/171)	0.0% (0/165)
Procedural blood loss (≥ 1,000 cc)	2.1% (4/187)	2.2% (4/183)	2.3% (4/176)	2.3% (4/171)	2.4% (4/165)
Aneurysm-related mortality	0.5% (1/187)	0.5% (1/183)	0.6% (1/176)	0.6% (1/171)	0.6% (1/165)

* Safety endpoints presented in this table are cumulative.

** Denominator is the number of patients eligible for analysis including patients with a major adverse event or patients with sufficient follow-up in the absence of a MAE for each study visit.

1.2.2 Device-Related Serious Adverse Events

Site-reported Serious Adverse Events (SAEs) are summarized in **Table 19**. The MedDRA (Medical Dictionary for Regulatory Activities) codes were used to categorize all the site reported SAEs. The percentage of SAEs at each time point was calculated as patients with events over the patients eligible for each follow-up visit.

The incidence of device-related SAEs was 4.8% in the first year, excluding the perioperative period. A lower rate (1.1% to 3.7%) was observed at all other intervals through 5 years, including the perioperative period. The majority of device-related SAEs (e.g., stent-graft endoleaks, implant vascular graft occlusions, aortic stent-graft thrombosis, AAA enlargement) were included in the secondary effectiveness endpoint analysis. Aside from these device-related events, prostatic cancer, phlebothrombus of lower extremities, and thromboembolism occurred in 1 patient each.

Table 19. Device-Related Serious Adverse Events by Study Period

n (%)[a]	Day 0-30 N=190	Day 31-Year 1 N=188	Year 1-2 N=178	Year 2-3 N=161	Year 3-4[b] N=149
Any device-related SAE	2 (1.1%)	9 (4.8%)	4 (2.2%)	6 (3.7%)	4 (2.7%)
Aortic stent-graft thrombosis	-	5 (2.7%)	-	-	-
Stent-graft endoleak	-	-	2 (1.1%)	5 (3.1%)	3 (2.0%)
Fever	2 (1.1%)	1 (0.5%)	-	-	-
Vascular graft occlusion	-	4 (2.1%)	1 (0.6%)	1 (0.6%)	-
Prostatic cancer	-	-	-	1 (0.6%)	-
Abdominal aortic aneurysm enlargement	-	-	-	2 (1.2%)	-
Lower extremities-phlebothrombus of	-	-	1 (0.6%)	-	-
Thromboembolism	-	-	-	-	1 (0.7%)

a. N at each time point includes patients who had an event or who had sufficient follow-up in the absence of an event at each time point
b. 4-year data through December 29, 2017

1.2.3 Procedure-Related Serious Adverse Events

The incidence of procedure-related SAEs was 10.5% within the first 30 days of the index procedure, and decreased following the perioperative period to an annual rate of approximately 3% or lower (**Table 20**). Procedure-related SAEs that occurred in more than one patient included fever (n=3, 1.6%) and other events (e.g., stent graft endoleaks, vascular graft occlusions, aortic stent graft thrombosis, AAA enlargement) that were included in the secondary effectiveness endpoint analysis. Other events primarily occurred within 30 days of the index procedure and in no more than one patient each (e.g., anemia, acute myocardial infarction, constipation, subileus).

Table 20. Procedure-Related Serious Adverse Events by Study Period

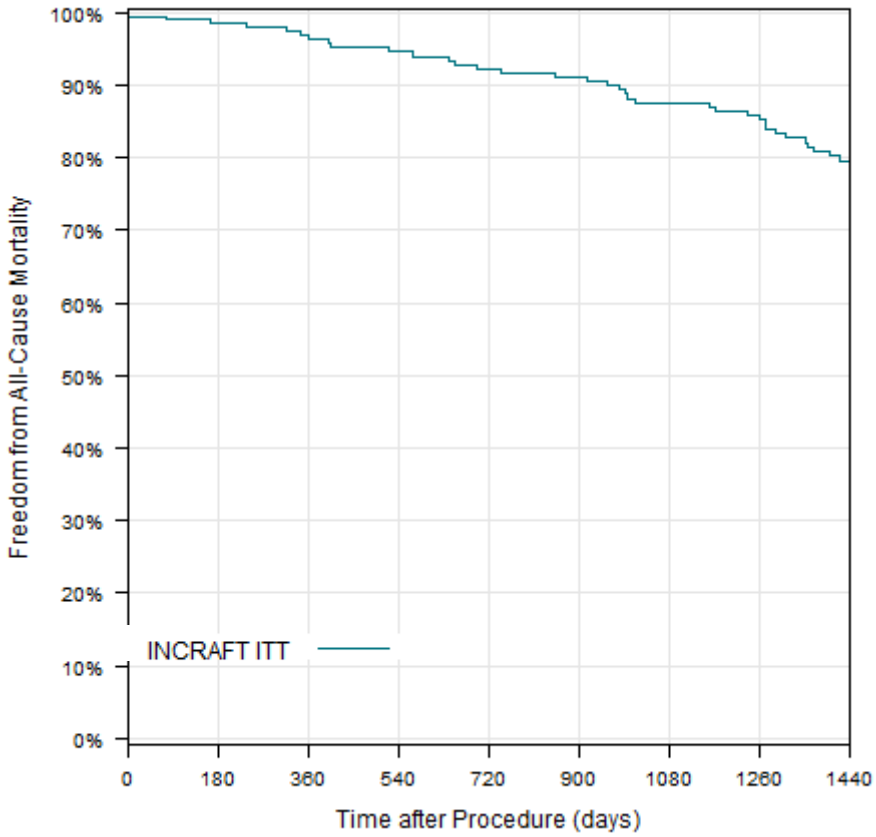
n (%)[a]	Day 0-30 N=190	Day 31-Year 1 N=188	Year 1-2 N=178	Year 2-3 N=161	Year 3-4[b] N=149
Any procedure-related SAE	20 (10.5%)	4 (2.1%)	1 (0.6%)	5 (3.1%)	4 (2.7%)
Anemia	1 (0.5%)	-	-	-	-
Myocardial infarction acute	1 (0.5%)	-	-	-	-
Constipation	1 (0.5%)	-	-	-	-
Subileus	1 (0.5%)	-	-	-	-
Aortic stent-graft thrombosis	-	2 (1.1%)	-	-	-
Fever	3 (1.6%)	-	-	-	-
Stent-graft endoleak	-	-	-	3 (1.9%)	2 (1.3%)
Bleeding of suture site	1 (0.5%)	-	-	-	-
Contrast media reaction	1 (0.5%)	-	-	-	-
Procedural haemorrhage	1 (0.5%)	-	-	-	-
Vascular graft occlusion	-	1 (0.5%)	1 (0.6%)	1 (0.6%)	1 (0.7%)
Creatinine high	1 (0.5%)	-	-	-	-
Fluid overload	-	1 (0.5%)	-	-	-
Neuropathy	1 (0.5%)	-	-	-	-
Syncopal attack	1 (0.5%)	-	-	-	-
Renal impairment	1 (0.5%)	-	-	-	-
Renal insufficiency	1 (0.5%)	-	-	-	-
Urethral stricture traumatic	1 (0.5%)	-	-	-	-
Urinary retention	1 (0.5%)	-	-	-	-
Acute respiratory decompensation	1 (0.5%)	-	-	-	-
Acute respiratory failure	1 (0.5%)	-	-	-	-
Hypoxia	1 (0.5%)	-	-	-	-
Aneurysm enlargement	-	-	-	2 (1.2%)	1 (0.7%)
Occlusion	1 (0.5%)	-	-	-	-
Popliteal artery occlusion	-	-	1 (0.6%)	-	-

a. The denominator, N, at each time point includes patients who had an event or who had sufficient follow-up in the absence of an event at each time point
b. 4-year data through December 29, 2017

1.2.4 All-Cause Mortality

A Kaplan-Meier analysis of freedom from all-cause mortality was performed (**Figure 5**). For the INCRAFT cohort, freedom from all-cause mortality was estimated to be 99.5% at 30 days, 98.4% at 180 days, 96.8% at 1 year, 92.2% at 2 years, 87.6% at 3 years and 79.5% at 4 years. There was one aneurysm-related mortality, which occurred 2-days post-operatively (**Section 2.2.3**).

Figure 5. Kaplan-Meier Analysis: Freedom from All-Cause Mortality through 4 years



INCRAFT Cohort	Time After Procedure						
	0 Days	**1-30 Days**	**31-180 Days**	**181-360 Days**	**361-720 Days**	**721-1080 Days**	**1081-1440 Days**
# At Risk	190	188	182	177	161	149	115
# Censored	0	1	4	2	8	4	21
# Events	0	1	2	3	8	8	13
Survival	100.0%	99.5%	98.4%	96.8%	92.2%	87.6%	79.5%
Peto SE¥	0.0%	0.5%	0.9%	1.3%	2.0%	2.5%	3.1%

¥ Peto's formula utilizing non-parametric weights accounting for number of patients at risk was used in calculating the standard error.

2. Effectiveness Results

2.1 Primary Effectiveness

The analysis of effectiveness was based on the 190 patients enrolled in the study for peri-procedural components of the composite effectiveness endpoint, and the 177 evaluable patients for the 12-month components of the composite effectiveness endpoint. Key effectiveness outcomes are presented in **Table 21**.

The rate of successful aneurysm treatment at 1 year was 87.9% (152/173). There were no aneurysm enlargements, migrations, or aneurysm sac ruptures noted out to 1 year, as is shown in **Table 21**. The primary effectiveness endpoint met the pre-defined 80% performance goal.

Overall, twenty-one patients did not meet the primary effectiveness endpoint (152/173). At the conclusion of the index procedure the rate of technical success was 94.1% (176/187). A denominator of 187 was used because there were three patients that had unknown types of endoleak reported so they were excluded from the analysis. The reasons for not achieving technical success were related to 2 devices that were deployed at the unintended location (1 resulting in an SMA tear requiring stent placement and the other not resulting in any procedure-related or device-related adverse event) and 9 Type I endoleaks present at the conclusion of the procedure. Both a technical and clinical review of the 2 cases related to deployment were performed. It revealed that the user failed to stabilize the white handle component of the INCRAFT delivery system during the pulling process of the fixation release wire. The Type I endoleaks all resolved by the 1-month follow-up.

Additionally, there were 2 conversions to open surgery, 3 Type I endoleaks, and 7 graft occlusions noted through 1 year. These events were all adjudicated by the Clinical Events Committee (CEC) to meet the definition of unsuccessful aneurysm treatment. Please note that the protocol definition of graft occlusion implies that the vessel is 100% occluded. Additional information regarding these events is located in the respective sections below.

Table 21. Primary Effectiveness Endpoint Results

	INCRAFT		
Primary Endpoint	**Total Patients (N = 190)¥**		**95% CI**
Primary Composite Effectiveness Endpoint	87.9%	(152/173)	(83.0%, -)
Successful Aneurysm Treatment to 1 year composite Rate†			
Technical Success (Peri-procedure) ‡	94.1%	(176/187)	
Successful insertion of the delivery system	100.0%	(190/190)	
Successful deployment of device at intended location	98.9%	(188/190)	
Graft patency	100.0%	(190/190)	
Absence of Type I endoleak	95.2%	(178/187)	
Absence of Type III endoleak	100%	(187/187)	
Absence of sac rupture	100.0%	(190/190)	
Absence of postoperative aneurysm enlargement	100.0%	(173/173)	
Absence of postoperative migration	100.0%	(172/172)	
Absence of postoperative conversion	98.9%	(173/175)	
Absence of postoperative sac rupture	100.0%	(175/175)	
Absence of postoperative Type I/III endoleak	98.3%	(170/173)	
Absence of postoperative graft occlusion	96.0%	(168/175)	

† Successful Aneurysm Treatment is described as the composite endpoint of the following:

- Absence of post-operative aneurysm enlargement (growth > 5 mm) or migration (> 10 mm), compared to the one month size measurement at any time up to 1 year;
- Absence of post-operative conversion to open surgery, sac rupture, endoleak Type I/III, or graft occlusion (including unilateral or bilateral limb occlusion) at any time up to 1 year;
- Considered a Technical Success as defined below.

‡ Technical Success at the conclusion of the index procedure, defined as successful insertion of the delivery system through the vasculature and successful deployment of the device at the intended location. The endovascular graft must be patent, with absence of types I or III endoleaks or aneurysm sac rupture, at the time of procedure completion as confirmed by angiography or other imaging modality.

¥ Denominator is the number of patients evaluable for this endpoint.

2.2 Secondary Effectiveness Endpoints

Secondary effectiveness endpoints are summarized in **Table 22** and discussed in the respective sections**.** The data presented are the number of patients with the event observed during each time point. Patients with fractures and migration identified in earlier time points will continue to be included in the numerator and denominator for later time points; however, data are not cumulative.

Notably, rates of effectiveness-related events such as transrenal stent fractures, patency-related events, and aneurysm expansion are higher than typically reported for a pivotal study performed in the US for the evaluation of an endovascular graft system intended for infrarenal abdominal aortic aneurysm repair.

The following paragraphs describe observations through 4 years. Please note that reported device malfunctions are not included in this summary (See **Section 2.2.2**).

Technical success at 1 month, defined in the INSPIRATION study as graft patency with the absence of Type I or III endoleaks or aneurysm sac rupture confirmed by imaging was 100%. There was 1 (0.5%) aneurysm-related mortality at 1 month and no additional aneurysm-related mortality occurred after the 1 month time point through 4 years.

At 1 month, there were no new Type I/III/IV endoleaks. The Type Ia endoleaks observed in 9 patients at the procedure (9/190, 4.7%) were resolved by 1 month. All Type IV endoleaks observed post index procedure were resolved by 1 month. No incidences of stent fracture, patency-related events, or conversion to open surgery were reported by 1 month. There was 1 secondary intervention performed for vascular injury post-index procedure.

At 6 months, there were 3 patients with at least 1 transrenal stent fracture (total of 7 fractures), 4 stent graft occlusions (1 complete device occlusion, 3 occlusions of an iliac limb), 1 conversion to open surgery and 5 secondary interventions. There were no incidences of Type I or III endoleaks, aneurysm enlargement, or migration. The 4 patients with stent graft occlusion resolved with secondary intervention.

At 1 year, there were 3 new Type I endoleaks, 8 patients with at least 1 transrenal stent fracture (total of 14 fractures), 3 stent graft occlusions of an iliac limb, 1 conversion to open surgery and 8 secondary interventions. The 3 patients with stent graft occlusions of an iliac limb resolved with secondary intervention. There were no incidences of aneurysm enlargement or stent migration.

At 2 years, there were 11 new aneurysm enlargements, 5 Type I endoleaks (including 1 persistent), 10 patients with at least 1 transrenal stent fracture (total of 22 fractures), 1 stent graft occlusion of an iliac limb, 1 proximal limb migration and 7 secondary interventions. The 1 patient with stent graft occlusion of an iliac limb resolved with secondary intervention.

At 3 years, there were 23 total aneurysm enlargements (including 10 aneurysm enlargements persisting from 2 years), 3 Type I endoleaks (including 1 persistent), 1 new Type III endoleak, 13 patients with at least 1 transrenal stent fracture (total of 26 fractures), 1 patient with complete device graft occlusion, 5 patients with proximal limb migrations and 12 secondary interventions. The 1 patient with stent graft occlusion resolved with secondary intervention.

At 4 years, there were 23 total aneurysm enlargements (including 19 aneurysm enlargements persisting from 3 years), 2 Type I endoleaks (including 1 peristent), 17 patients with at least 1 transrenal stent fracture (total of 31 fractures), 1 patient

with complete stent graft occlusion, 5 patients with proximal limb migrations and 8 secondary interventions. The 1 patient with stent graft occlusion resolved with secondary intervention.

For the duration of the study, no patients with stent fracture had clinical sequelae attributable to stent fracture(s), and there were no aneurysm sac ruptures.

Type II endoleaks, stenoses and kink events were not defined as secondary effectiveness outcomes per the protocol. Through 4-year follow-up, 101 patients (101/190, 53.2%) were observed with 108 Type II endoleaks, 15 patients (15/190, 7.9%) were observed with 17 stent graft stenosis, and 1 patient (1/190, 0.5%) was observed with 1 limb kink. Refer to the Endoleaks (**Section 2.2.6**) and Stent Graft Patency (**Section 2.2.9**) for discussion of these events.

Notable differences in reported outcomes between the US and Japan are provided in the subsequent sections, as applicable. In general, device-related event rates were higher in the US; 13.2% vs. 3.8% at 1 year, 20.0% vs. 11.8% at 2 years, 33.7% vs. 25.0% at 3 years, and 43.3% vs. 29.5% at 4 years. The event driving the differences throughout the duration of the study was transrenal stent fracture(s).

Table 22. Secondary Effectiveness Results

Secondary Effectiveness Endpoints	INCRAFT Patients (N = 190)							
	Peri-Procedure	1 Month	6 Months	1-Year	2-Years	3-Years	4-Year	Total
Technical success at 1 month ‡	N/A	100.0% (186/186)	N/A	N/A	N/A	N/A	N/A	N/A
Device-related events*	N/A	(0/181)	4.2% (7/167)	10.1% (16/159)	17.0% (24/141)	30.5% (40/131)	37.8% (42/111)	30.5% (58/190)
Device malfunction¥	N/A	(0/189)	(0/183)	1.1% (2/176)	1.2% (2/161)	2.0% (3/148)	2.4% (3/127)	5.3% (10/190)
Aneurysm sac rupture	N/A	(0/189)	(0/183)	(0/176)	(0/161)	(0/148)	(0/127)	(0/190)
Stent graft migration***	N/A	N/A	(0/177)	(0/172)	0.6% (1/154)	3.5% (5/141)	4.5% (5/112)	2.6% (5/190)
Endoleaks (Type I)	N/A	(0/186)	(0/175)	1.8% (3/167)	2.7% (4/149)	1.5% (2/131)	1.0% (1/102)	5.3% (10/190)
Endoleaks (Type III)	N/A	(0/186)	(0/175)	(0/167)	(0/149)	0.8% (1/131)	(0/102)	0.5% (1/190)
Endoleaks (Type IV)	N/A	(0/186)	N/A	N/A	N/A	N/A	N/A	N/A
Aneurysm enlargement	N/A	N/A	(0/176)	(0/173)	7.1% (11/155)	16.2% (23/142)	20.5% (23/112)	14.7% (28/190)
Fractures∞ ¥	N/A	(0/183)	1.7% (3/172)	4.9% (8/163)	6.8% (10/147)	9.5% (13/137)	14.9% (17/114)	8.9% (17/190)
Graft occlusion¥	N/A	(0/189)	2.2% (4/183)	1.7% (3/176)	0.6% (1/161)	0.7% (1/148)	0.8% (1/127)	5.3% (10/190)
Conversion to open surgery¥	N/A	(0/189)	0.5% (1/183)	0.6% (1/176)	(0/161)	(0/148)	(0/127)	1.1% (2/190)
Aneurysm-related mortality§	N/A	0.5% (1/190)	-	-	-	-	-	0.5% (1/190)
Delivery system malfunction	4.2% (8/190)	N/A	N/A	N/A	N/A	N/A	NA	4.2% (8/190)
Incidence of secondary interventions, or the need for secondary interventions, to repair vascular events or malfunctions	N/A	0.5% (1/189)	2.7% (5/183)	4.5% (8/176)	4.3% (7/162)	8.1% (12/148)	6.3% (8/127)	17.9% (34/190)
Incidence of secondary interventions, within 1 year post procedure needed to prevent the occurrence of a significant event	N/A	(0/189)	(0/182)	(0/176)	NA	NA	NA	N/A

Secondary Effectiveness Endpoints	INCRAFT Patients (N = 190)							
	Peri-Procedure	1 Month	6 Months	1-Year	2-Years	3-Years	4-Year	Total

* - For aneurysm enlargement, endoleaks, fractures, and migrations, denominators are based on evaluable data in CORE windows: 1 Month (post-procedure - 90 days); 6 Month (91 - 270 days); 12 Month (271 - 540 days) 2 Years (541 - 900 days), 3 Years (901 - 1260 days), 4 Years (1261 - 1620 days);

- For aneurysm sac ruptures, malfunctions, graft occlusions, conversions to open surgery, and secondary interventions, denominators are defined based on evaluable data in follow-up windows: 1 Month (procedure - 30 days); 6 Month (31 - 180 days); 12 Month (181 - 360 days) 2 Years (361 - 720 days), 3 Years (721 - 1080 days)

∞ - Patients with fractures and migration identified will continue to be included in the numerator and denominator for later time points

§ Aneurysm-related mortality was defined as a death from AAA rupture, or death within 30 days of open aortic surgical or endovascular repair or death from any subsequent procedure required to treat the same aneurysm. Not defined as device-related event as per protocol.

‡ Technical success at 1 month was defined as a patent endovascular graft with absence of Types I or III endoleaks or aneurysm sac rupture, up to 1 month post-procedure completion as confirmed by CT.

¥ A summary of conversions to open surgery, graft occlusions, device malfunctions and stent fractures are noted above table. Refer to **Section** 2.2.2 for a summary of device malfunctions.

*** The migrations seen through 4 years only include proximal limb migration, no migration of the bifurcate prosthesis.

2.2.1 Technical Success

For the INSPIRATION study, the definition of technical success at 1 month, is the endovascular graft must be patent, with absence of Types I or III endoleaks or aneurysm sac rupture, up to 1-month post-procedure completion as confirmed by CT or other imaging modality. The rate of technical success at 1 month was 100%.

2.2.2 Device Malfunctions

Device malfunction is defined as failure of a device to meet any of its performance specifications or otherwise perform as intended. In this study, a device malfunction was determined by the clinical site per the study protocol and may consist of a subset of events discussed in the sections for each endpoint in this document. Eighteen device malfunctions were reported by the clinical sites during the study through 4 years (**Table 23**). The data includes 8 delivery system malfunctions and 10 device malfunctions specific to the implanted components of the INCRAFT system.

Eight delivery system malfunctions were reported during the INSPIRATION clinical study at the time of the index procedure. Five of the 8 malfunctions were related to leakage in the aortic bifurcate hemostasis valve. Minor manufacturing process improvements have been implemented to reduce the potential for leakage in the aortic bifurcate hemostasis valve. The remaining 3 delivery system malfunctions were related to a high fixation release wire pull force, a component migration noted in the patient with deployment of the device not at the intended location, and a broken proximal sheath introducer respectively.

There were two devices deployed at the unintended location; however, only one was reported by the site as a delivery system malfunction. In the one observed case of high fixation release-wire pull-force, the device was successfully deployed at the intended location with no procedure-related or device-related adverse events.

Ten device malfunctions specific to the implant components of the INCRAFT were reported during the INSPIRATION clinical study at various time points. Device malfunctions were assessed at the discretion of the investigators; therefore, not all endpoint events were reported as device malfunctions. Please refer to the respective sections below for the totality of observations/events that occurred in the clinical study.

Table 23. Device Malfunctions through 4 Years

	Peri-Procedure % (n/N)	1 Month % (n/N)	6 Months % (n/N)	1 Year % (n/N)	2 Year % (n/N)	3 Year % (n/N)	4 Year % (n/N)
Device or Delivery System Malfunction	4.2% (8/190)	0% (0/189)	0% (0/183)	1.1% (2/176)	1.2% (2/161)	2.0% (3/148)	2.4% (3/127)

2.2.3 Aneurysm-Related Mortality

Aneurysm-related mortality (ARM) was defined as a death from AAA rupture, or death within 30 days of open aortic surgical or endovascular repair, or death from any subsequent procedure required to treat the same aneurysm. There was one (0.5%) ARM observed. This patient died 2 days after the index procedure due to a myocardial infarction. This incidence of death met the definition of aneurysm-related mortality because the death occurred within 30 days of the endovascular repair.

2.2.4 Aneurysm Sac Rupture

There have been no aneurysm sac ruptures reported in the study.

2.2.5 Migration

Device migration was defined as evidence of proximal or distal movement of the stent graft > 10 mm relative to fixed anatomical landmarks compared with the 1-month imaging measurement as assessed by the Core Lab. There were two different Core Labs used in the study; the measurements from baseline through 1-year were made by the first Core Lab and follow-up measurements (after 1-years and beyond) were made by the second Core Lab. The second Core Lab re-calculated the 1-month migration measurements due to changes in the baseline measurement process from the first Core Lab for all subsequent measurements after 1 year.

There were no aortic bifurcate migrations that meet the protocol definition. However, there were 2 patients that each had aortic bifurcate migration of 10 mm noted at the 3-year and the 4-year follow up visit, respectively. Both migrations were likely associated with neck dilatation.

In addition to aortic bifurcate migration, limb migration was also investigated in the study. Proximal iliac limb migration was defined as proximal movement greater than 10 mm of the distal margin of the iliac limb in relation to the hypogastric orifice. No limb migrations were observed by the 1-year follow-up visit. Five limb migrations were observed by the Core Lab beyond the 1 year time point through 4 years. All of the limb migrations were proximal limb migrations, and no limb separations were observed. The migration status at each time point are based on the images reviewed by the Core Lab. One of

the patients with limb migration at 3 years post procedure was observed with Type Ib endoleak, which resolved following placement of an additional limb.

The number and percent of device migrations at the study follow-up visits are presented in **Table 24.** The patients with adequate imaging to assess the migration is used for the denominator for the percentage calculation.

Table 24. Iliac Limb Migration through 4 Years

	Treatment to 12 Months % (n/N)	**1 Month % (n/N)**	**6 Months % (n/N)**	**12 Months % (n/N)**	**2 Year % (n/N)**	**3 Year % (n/N)**	**4 Year % (n/N)**
Iliac Limb Migration *	**0% (0/187)**	0% (0/187)	0% (0/177)	0% (0/172)	0.6% (1/154)	3.5% (5/141)	4.5% (5/112)

*: Patients with migration identified will continue to be included in the numerator and denominator for later time points.

2.2.6 Endoleaks

In the INSPIRATION Study, the Clinical Events Committee (CEC) adjudicated Type I, III and IV endoleaks. Types II and V endoleaks were not adjudicated by the CEC. A summary of endoleaks present at the end of each follow-up time point through 4 years is presented in **Table 25**.

Fifteen patients were observed with 16 Type Ia endoleaks. The Type Ia endoleaks observed in 9 patients at the procedure (4.7%) were resolved by 1 month with no secondary intervention. No aneurysm expansion attributable to Type 1a has been observed in the 9 patients with procedural Type 1a endoleaks. One patient with procedural Type 1a endoleak had aneurysm expansion attributed to Type II endoleak at 3-years. One patient with a procedural Type Ia endoleak that resolved by 1 month also later developed a new Type Ia endoleak during followup.

A total of seven (7) patients were observed to have Type Ia endoleaks during follow-up. Five (5) patients who were observed with Type Ia endoleaks during follow-up underwent standard secondary interventions to resolve the endoleak, including coil embolization and/or placement of aortic cuff, EndoAnchors, chimneys (i.e., proximal placement of stent grafts parallel to an aortic cuff to facilitate branch vessel perfusion and exclusion of the aneurysm), and/or stents. No secondary interventions were performed on the remaining 2 Type Ia endoleaks that were observed during follow-up and no subsequent imaging is available for these patients. Two aneurysm expansions were related to the observation of post-procedural Type Ia endoleaks. One patient had an aneurysm expansion with secondary intervention to address the Type Ia endoleak. The second patient had both a Type Ia and Type II endoleak, which contributed to aneurysm enlargement; both endoleaks had a secondary intervention.

Three (3) patients were identified with Type 1b endoleaks; 1 at 2 years and 2 at 3 years. One of the patients that had limb migration noted at 3 years developed a Type Ib endoleak. This patient received an additional stent graft to resolve the endoleak. The other two Type Ib endoleaks observed underwent a secondary intervention to resolve the endoleak, namely placement of additional stent grafts. One patient had both a Type Ib and Type II endoleak which contributed to aneurysm enlargement; both endoleaks had a secondary intervention.

One hundred and eight (108) Type II endoleaks were identified in 101 patients in the study through 4 years, which account for majority of the endoleaks reported. Seventeen of the Type II endoleaks observed in 15 patients (17/108, 15.7%) were treated with a secondary intervention that included coil and/or glue embolization. As noted in the Change in Aneurysm Diameter section below (**Section 2.2.7**), 24 patients with Type II endoleaks (24/101, 23.8%) were associated with aneurysm expansion greater than 5 mm. Eleven (11) of the 24 patients with Type II endoleaks with aneurysm expansion have undergone a secondary intervention to address the observations.

One (1) patient was observed with a Type IIIb endoleak at the 3-year follow-up. The endoleak was related to a fabric tear in the left limb. The endoleak was successfully treated by placement of an additional limb component. The Medical Monitor stated that the limbs were in a “barber pole” configuration with the two limbs twisted about one another (i.e., limbs were crossed two times), which may have contributed to the fabric tear. No Type IIIa endoleaks have been observed to-date. There was no aneurysm enlargement observed in the patient with Type III endoleak.

The procedural Type IV endoleak occurrence rate, as adjudicated by the Clinical Events Committee, was 17.4% (33 Type IV endoleaks). Seven of those Type IV endoleaks were resolved at discharge and the remaining 26 resolved by the 1-month time point without a secondary intervention.

There was 1 patient reported with a Type V endoleak at 3 years and currently persists through the latest follow-up visit. This patient had an aneurysm expansion greater than 5 mm, which was attributed to endotension.

There were some differences in the rates of reported Type I or III endoleaks between the US and Japan; 1.8% vs. 1.9% at 1 year, 4.1% vs. 0% at 2 years, 1.2% vs. 4.2% at 3 years, and 0% vs. 2.6% at 4 years.

Table 25. Number of Patients with Endoleaks Reported through the 4 Year Follow-Up Visit

	Post-Procedure Day 0[A]	Discharge	1-Month	6-Month	1-Year	2-Year	3-Year	4-Year	Total Patients (Endoleaks)
# with Adequate Imaging	190	190	186	175	167	149	131	102	
Endoleaks (Total)[B,C]	90	74	72	68	64	66	58	49	167
Type Ia *(New + Persistent)* *Total*	(9 + 0) 4.7%	(0 + 6) 3.2%	-%	-%	(3 + 0) 1.8%	(3 + 1) 2.7%	(0 + 1) 0.8%	(1 + 1)[D] 1.9%	15 (16)
Type Ib *(New + Persistent)* *Total*	-%	-%	-%	-%	-%	(1 + 0) 0.7%	(2 + 0) 1.5%	-%	3 (3)
Type II *(New + Persistent)* *Total*	(42 + 0) 22.1%	(4 + 34) 20.0%	(47 + 25) 38.5%	(5 + 63) 37.8%	(1 + 60) 35.7%	(5 + 56) 39.1%	(1 + 52) 38.1%	(2 + 44) 39.3%	101 (108)
Type IIIb *(New + Persistent)* *Total*	-%	-%	-%	-%	-%	-%	(1 + 0) 0.8%	-%	1 (1)
Type IV *(New + Persistent)* *Total*	(33 + 0) 17.4%	(0 + 26) 13.7%	-%	-%	-%	-%	-%	-%	33 (33)
Type V[E] *(New + Persistent)* *Total*	-%	-%	-%	-%	-%	-%	(1 + 0) 0.8%	(0 + 1) 1.0%	1 (1)
Unknown Causes[F] *(New + Persistent)* *Total*	(2 + 0) 1.1%	(0 + 2) 1.1%	-%	-%	-%	-%	-%	-%	2 (2)
Other[G] *(New + Persistent)* *Total*	(3 + 0) 1.6%	(0 + 2) 1.1%	-%	-%	-%	-%	-%	-%	3 (3)

[A] Visits windows are defined as: At Procedure (0 days); At Discharge (1-discharge); 1 Month (discharge - 90 days); 6 Months (91 - 270 days); 1 Year (271 - 540 days); 2 Years (541 - 900 days); 3 Years (901 - 1260 days); 4 Years (1261 - 1620 days);

[B] Endoleaks are presented in subsequent visit windows following discovery until resolved.

[C] The 'New' and 'Persistent' row results reported for each endoleak subtype represent the number of patients with an endoleak in that category. In cases where a patient had more than one endoleak, the total number of endoleaks is presented in parentheses.

[D] CEC adjudication of the new Type 1A endoleak presented at the 4 year window was not finalized by the 29Dec17 database lock. Subtype information not reported by site. Categorization as a Type 1A based on preliminary adjudication data.

[E] Type V endoleaks identified via Medical Monitor review of database.

[F] Unknown Causes category includes two endoleaks at procedure, one endoleak in patient and one in patient where type could not be determined due to poor or inconclusive imaging.

[G] Other category includes one endoleak that was adjudicated as both Type II and Type IV and two endoleaks in two patients that were adjudicated as not Type I or Type III.

2.2.7 Change in Aneurysm Diameter

Per the study protocol, aneurysm enlargement is defined as growth of the aneurysm sac greater than 5 mm compared to the 1-month size measurement.

Patients with aneurysm expansion at any time point will continue to be reported in subsequent time points if the aneurysm size meets the definition of expansion. There were no aneurysm enlargements observed by the Core Lab at 6 months and 1 year. Eleven patients (7.1%) were observed with aneurysm enlargement at 2 years. At 3 years, 23 patients (16.2%) were observed with aneurysm enlargement, including 13 new enlargements and 10 ongoing enlargements from previous visit. At 4 years, 23 patients (20.5%) were observed with aneurysm enlargement, including 4 new enlargements and 19 ongoing enlargements from previous visit. Aneurysm regression (> 5 mm) was 22.7% at 6 months, 37.6% at 1 year, 36.8% at 2 years, 38.0% at 3 years, and 41.1% at 4 years.

The majority of the aneurysm sac enlargements were deemed likely attributable to Type II endoleaks (24/28). Three aneurysm expansions were deemed likely attributable to Type I endoleak. One enlargement had no endoleak observed and was classified as endotension. **Table 26** provides a summary of change in aneurysm diameter through 4-year follow-up as assessed by the Core Lab. There were 2 Core Labs utilized during the study. The measurement processes for aneurysm enlargement were uniform across the two Core Labs. **Table 27** provides further detail on the amount of aneurysm enlargement.

Aneurysm enlargement was the only event that had a consistently lower rate in the US as compared to Japan; 0% vs. 0% at 1 year, 6.9% vs. 7.5% at 2 years, 14.0 % vs. 20.4% at 3 years, and 17.9% vs. 24.4% at 4 years.

Table 26. Aneurysm Diameter Change through 4 Year Follow-Up

	6 Months	**1 Year**	**2 Year**	**3 Year**	**4 Year**	**Total***
Aneurysm diameter change from 1 month						
Aneurysm enlargement (increase > 5mm)	0% (0/176)	0% (0/173)	7.1% ((11 + 0)**/155)	16.2% ((13 + 10)/142))	20.5% ((4 + 19)/112)	14.7% (28/190)
Aneurysm stable (≤5mm regression/ enlargement)	77.3% (136/176)	62.4% (108/173)	56.1% (87/155)	45.8% (65/142)	38.4% (43/112)	
Aneurysm regression (decrease > 5mm)	22.7% (40/176)	37.6% (65/173)	36.8% (57/155)	38.0% (54/142)	41.1% (46/112)	

* Descriptive statistics presented in the Total column are for the maximum change in aneurysm diameter observed among patients with one or more value > 5 mm.

**(New + Persistent)

Table 27. Amount of Aneurysm Enlargement through 4 year Follow-Up

Measures (mm)	2 Years	3 Years	4 Years	Total*
Mean (SD)	9.0 (4.7)	9.9 (4.6)	11.1 (4.1)	11.2 (4.8)
Median	8.1	9.1	9.7	10.2
Range (min, max)	5.3, 22.4	5.3, 26.0	6.6, 20.9	(5.3, 26.0)

*Descriptive statistics presented in the Total column are for the maximum change in aneurysm diameter observed among subjects with one or more value > 5 mm

2.2.8 Stent Graft Integrity

Transrenal stent strut fractures were reported by the Core Lab based on the images received from the site. Upon review of patient images by the Core Lab, a total of 17 patients with stent strut fractures were observed on the follow-up (X-ray) imaging through 4 years. Three patients with stent strut fracture were observed at 6 months, five additional patients at 1 year, two additional patients at 2 years, three additional patients at 3 years, and four more patients at 4 years. A summary of the observed stent strut fractures through 4 years is presented in **Table 28**.

There were differences in the rates of reported fracture(s) between the US and Japan; 6.4% vs. 1.9% at 1 year, 9.6% vs. 1.9% at 2 years, 13.6 % vs. 2.0% at 3 years, and 21.7% vs. 4.4% at 4 years. There were 2 patients with a reported fracture in Japan as compared to 15 in the US through 4 years.

In the 17 patients with stent strut fracture confirmed by the Core Lab, one stent strut fracture in one patient was initially identified by the site. For the remaining 16 patients, stent strut fractures were identified by the Core Lab only.

Table 28. Summary of Stent Strut Fractures through 4 Years

	1 Month	6 Months	1 Year	2 Year	3 Year	4 Year
Number of Patients with Imaging adequate to assess Fractures	183	172	163	144	132	108
Number of Patients Newly Identified with at least 1 fracture	0	3	5	2	3	4
Cumulative Number of Patients with a fracture	0	3	8	10	13	17
Cumulative Number of Fractures	0	7	14	22	26	31

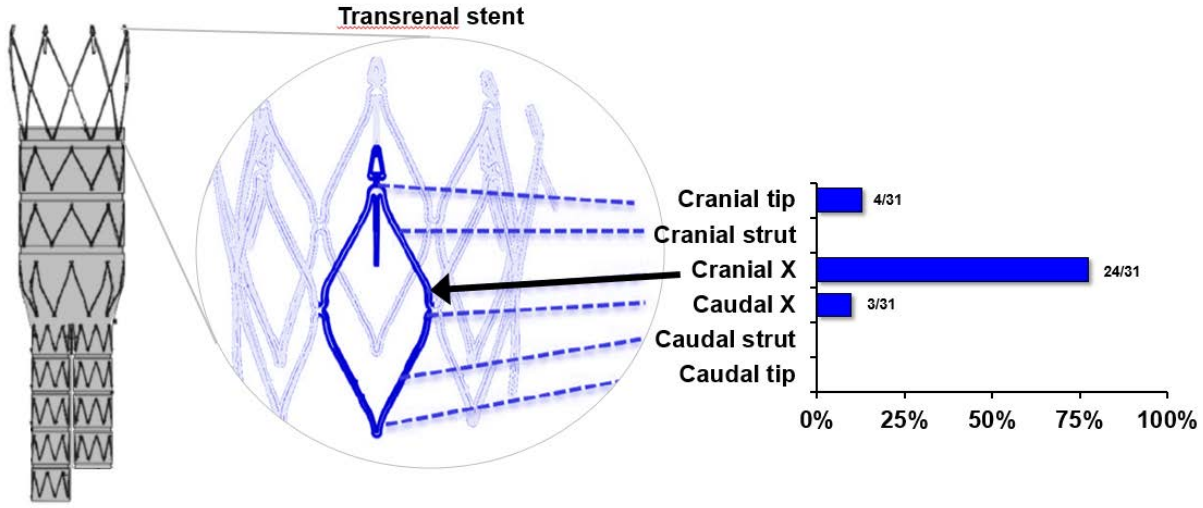
Among the 17 patients through 4 years, 12 patients had a single fracture, 2 patients had two fractures, 1 patient had three fractures and 2 patients had six fractures. Among the 5 patients with more than one stent strut fracture, 4 patients were observed with additional stent strut fractures following the time point that initial fractures were first observed, as shown in **Table 29.**

Table 29. Patients with Multiple Stent Strut Fractures at Follow-Up (N = 5)

	Total Number of Fractures at Each Follow Up Visit				
	6 Months	**1 Year**	**2 Year**	**3 Year**	**4 Year**
Subject A	1	1	1	1	2
Subject B	1	1	3	Not available	Not available
Subject C	0	1	5	6	6
Subject D	5	6	Not available	Not available	Not available
Subject E	0	2	2	2	2

All fractures observed were located at the transrenal stent, the stent component at the cranial end of the bifurcate implant which is not covered by the graft. Among the 17 patients with fractures through 4 years, the majority of fractures (24/31) were located at the "Cranial X" location of the stent, with 4 fractures at the "Cranial tip" location and 3 fractures at the "Caudal X" location (**Figure 6**). In 3 of the 5 patients with more than one stent fracture, the fractures resulted in disjointed stent segments (i.e., a stent segment that is not attached to the rest of the implant). There were a total of five disjointed segments through 4 years, with one patient having one disjointed segment and two patients with two disjointed segments. Four of these five disjointed segments included the fixation barb and one disjointed segment was a linear portion of a stent strut. Across available imaging through 4 years, the disjointed segments remained at the original location, and there was no strut embolization.

Figure 6: Location of All Stent Strut Fractures in INSPIRATION



There have been no known clinical sequelae or secondary interventions associated with the observation of stent strut fracture(s) reported through 4-

years. Specifically, no aortic bifurcate migration, Type Ia endoleaks, aneurysm sac enlargements or aneurysm rupture were attributed to the presence of fractures. There were three patients with stent strut fractures who had pre-existing and/or concurrent clinical events, which were assessed by the Medical Monitor to be independent of the transrenal stent strut fractures:

- Two patients with stent strut fractures had aneurysm growth of greater than 5 mm during the study. In both patients, the aneurysm enlargement was attributed to concurrent Type II endoleaks, independent of the strut fractures in the transrenal stent.
    - One patient had 6 fractures that developed from Year 1 through Year 4.
        - This patient had a non-INCRAFT aortic cuff/extension deployed during the initial procedure, which may or may not have contributed to the observed fractures.
        - An aneurysm enlargement of greater than 5 mm and a Type II endoleak were detected at the 3-year visit. The Type II endoleak resolved without any intervention by the Year 4 visit.
        - A new Type Ia endoleak was detected at Year 4. The Type Ia endoleak, which remained untreated, and the aneurysm enlargement were ongoing as of the latest follow up. This endoleak was assessed by the Medical Monitor as not attributed to the stent strut fracture as it was unaccompanied by aortic bifurcate migration.
        - Two additional fractures were observed at Year 5 for a total of 8 fractures.
    - The second patient had a single stent strut fracture at Year 4, a Type II endoleak that was first detected at 6 months, and aneurysm enlargement that started in Year 3 which became greater than 5 mm by Year 4.
- One patient with a single stent strut fracture at Year 3 had aortic bifurcate movement of 10 mm in Year 4. This movement (just under the > 10 mm threshold of protocol-defined migration) occurred steadily from 6 months through 4 years (7 mm of movement prior to stent fracture) and was attributed to dilatation of the aortic neck.

A root-cause investigation including non-clinical testing indicated that the primary cause of the observed transrenal stent fractures was likely cardiac-induced cyclic axial deformation. The root cause investigation has not identified any patient anatomical, demographic, or procedural related factors that may correlate with an increased risk of fracture or fracture propagation.

2.2.9 Stent Graft Patency

Per the INSPIRATION clinical study protocol, a stent graft occlusion was defined as a complete absence of flow within the stent graft. A stenosis was

defined as patency within the stent graft that was less than 100% obstructed. In the study, twenty-four patients (24/189, 12.6%) were observed with an occlusion or other patency-related event.

Ten (10) patients were observed by the site with stent-graft occlusions. Most of the occlusions occurred early (within 1 year). All patients underwent secondary interventions, resolving the stent graft occlusions; no occlusions reoccurred after the interventions. Two patients had complete occlusion of the aortic bifurcate component and both iliac limbs noted at 6 months and 3 years, respectively. One of the patients was converted to open repair 173 days post procedure. Thrombosis of the entire stent graft was observed in the second patient at the 2 year follow-up, which progressed to complete occlusion of the implant, observed 781 days post procedure. The INCRAFT device was relined with commercially available devices to restore perfusion to the lower extremities. No additional secondary intervention was completed to address thrombosis or occlusion for this patient.

The other 8 patients had limb occlusions with 7 patients having single limb occlusion (3 at 6-months, 3 at 1 year, and 1 at 2 years). One patient at 4 years developed a bilateral limb occlusion and underwent an axillo-bifemoral bypass procedure to address the occlusion. All occlusion patients underwent secondary intervention, resolving the occlusion. The occlusions did not recur after the interventions. The secondary interventions completed to address the limb occlusions in the 8 patients include the following: fem-fem bypass (3), right to left axillo-bifemoral bypass (1), relining of the INCRAFT device with competitor limbs (1), placement of 1 stent/embolectomy (1), placement of 1 stent/thrombolysis/ thrombectomy/PTA (1), placement of 1 stent/angioplasty (1), and placement of 2 stents/thrombolysis/thrombectomy/PTA/fem-fem bypass (1).

There were some differences in the rates of reported occlusions between the US and Japan; 2.5% vs. 0% at 1 year, 0.9% vs. 0% at 2 years, 1.0% vs. 0% at 3 years, and 1.3% vs. 0% at 4 years.

Fifteen (15) patients were reported by the site with 17 stent graft stenoses. All stent graft stenoses were observed in the iliac limbs. Seven patients underwent secondary interventions to resolve the stenoses and 8 patients did not require an intervention. The stenoses did not recur after the interventions. The secondary interventions completed to address stent graft stenosis or thrombus include the following: conversion to open repair (1), placement of 1 stent (3), placement of 1 stent/angioplasty (1), placement of 3 stents/thrombectomy (1), and angioplasty (1).

One (1) patient was observed with a limb kink by the site at the 3-year visit. The patient underwent stent placement to resolve the kink. The kink did not recur after the intervention.

All patients met the selection criteria for the study, including absence of significant aortic or iliac mural thrombus, plaque, or calcification that would compromise fixation or seal of the device, as well as absence of coagulopathy, bleeding disorder, or other hypercoagulable state. A retrospective analysis of the clinical and anatomical characteristics of all patients with patency-related events did not identify contributing causes unique to the patients with patency-related events.

Table 30 provides a summary of all patients with patency-related events including stent graft occlusions, graft stenoses and limb kink.

Table 30. Patency Related Events through 4 Years

	INCRAFT					
	1 Month	**6 Months**	**1 Year**	**2 Years**	**3 Years**	**4 Years**
Patients with Visit Data	189	182	177	162	148	129
Occlusion	0	4	3	1	1	1
Stenosis	0	4	8	1	3	1
Device kink	0	0	0	0	1	0

2.2.10 Conversion to Open Surgery

Two patients underwent conversion to open surgery within the 4-years follow-up time point due to patency-related events, specifically complete device occlusion and mural clot in both iliac limbs of the INCRAFT, respectively. Potential contributing factors to the conversion to open surgery in these cases are discussed below:

One patient at 173 days post-procedure was converted to open surgery due to complete occlusion of the aortic bifurcate component and both iliac limbs. This patient also had mild stenoses at the proximal limbs on completion angiography at the index procedure and possible hypercoagulability syndrome (prostate cancer).

One patient was converted to open surgery at 206-days post procedure due to bilateral iliac limb stenosis.

While the patient with bilateral iliac limb stenosis had no clinical or anatomic findings identified as factors for the thrombotic event, extensive atherosclerotic popliteal disease was present in the patient with complete occlusion of the stent graft that was converted to open surgery at 173 days post-procedure.

Regarding the patients with conversion to open surgery, the patients' medical history or prescribed medications might have predisposed them to thrombosis of the stent graft. Both patients met the selection criteria for the study, including absence of significant aortic or iliac mural thrombus, plaque or calcification that would compromise fixation and seal of the device.

Additionally, an axillo-bifemoral bypass was completed to address a patency-related event. Please reference the stent graft patency **Section 2.2.9** for additional details regarding these interventions.

2.2.11 Secondary Interventions

A total of 34 patients underwent 47 secondary interventions through 4 years to repair the device or aneurysm**.** The majority of secondary interventions were to address patency-related events and Type II endoleaks. A summary of the secondary interventions is presented in **Table 31.** Secondary interventions for patency-related events and endoleaks were discussed in their respective sections.

Two patients underwent secondary interventions that were not discussed in the preceding sections, 1 for vascular injury and 1 for suture site bleeding. During the procedure, the first patient was treated for a superior mesenteric artery intimal tear with placement of a stent resolving the tear. This patient was considered a technical failure (see **Section 2.1**). The second patient underwent a secondary intervention for the Type II endoleak at 2-years post procedure. Following the secondary intervention, bleeding of vascular access site was observed and a fem-stop device was applied to the site resolving the bleed.

There were some differences in the rates of reported secondary interventions between the US and Japan; 6.6% vs. 0% at 1 year, 5.5% vs. 1.9% at 2 years, 8.1% vs. 8.2% at 3 years, and 6.3% vs. 6.4% at 4 years.

Table 31. Summary of Reasons for Secondary Interventions through 4 Years

	1-Month	**6-Month**	**1-Year**	**2-Year**	**3-Year**	**4-Year**	**Total**
Number of Patients Eligible	189	182	177	162	148	129	
Patients with Any Intervention	1 0.5% (1/189)	5 2.7% (5/182)	8 4.5% (8/177)	7 4.3% (7/162)	12 8.1% (12/148)	8 6.2% (8/129)	34
Number of Interventions	1	5	9	9	14	9	47
Secondary Intervention for Stent graft occlusion*	0 (0) 0% (0/189)	3 (3) 1.6% (3/182)	4 (4) 2.3% (4/177)	1 (1) 0.6% (1/162)	1 (1) 0.7% (1/148)	1 (1) 0.8% (1/129)	10 (10) ± 5.3% (10/190)
Conversion to open surgery	0	1±	0	0	0	0	1
Fem-Fem Bypass	0	1	1	1	0	0	3

	1-Month	6-Month	1-Year	2-Year	3-Year	4-Year	Total
Number of Patients Eligible	189	182	177	162	148	129	
Patients with Any Intervention	1 0.5% (1/189)	5 2.7% (5/182)	8 4.5% (8/177)	7 4.3% (7/162)	12 8.1% (12/148)	8 6.2% (8/129)	34
Number of Interventions	1	5	9	9	14	9	47
Right to Left Axillo-bifemoral bypass	0	0	0	0	0	1	1
1 Stent/embolectomy	0	0	1	0	0	0	1
1 Stent/thrombolysis/ thrombectomy/ PTA	0	0	1	0	0	0	1
1 Stent/angioplasty	0	1	0	0	0	0	1
2 Stents/ thrombolysis/ thrombectomy/PTA/ Fem-Fem Bypass	0	0	1	0	0	0	1
Relining of INCRAFT graft with competitor limbs	0	0	0	0	1	0	1
Secondary Intervention for Stent graft stenosis or thrombus[*, β]	0 (0) 0% (0/189)	1 (1) 0.5% (1/182)	5 (5) 2.8% (5/177)	1 (1) 0.6% (1/162)	0 (0) 0% (0/148)	0 (0) 0% (0/129)	7 (7) 3.7% (7/190)
Angioplasty	0	0	1	0	0	0	1
Meds/Conversion to open surgery	0	0	1	0	0	0	1
1 Stent	0	1	2	0	0	0	3
1 Stent/Angioplasty	0	0	1	0	0	0	1
3 Stents/thrombectomy	0	0	0	1	0	0	1
Secondary Intervention for Type Ia Endoleak[*]	0 (0) 0% (0/189)	0 (0) 0% (0/182)	0 (0) 0% (0/177)	4 (4) 2.5% (4/162)	2 (2) 1.4% (2/148)	0 (0) 0% (0/129)	5 (6)[∞] 2.6% (5/190)
Coil embolization	0	0	0	1	0	0	1
Aortic cuff	0	0	0	1	0	0	1
Aortic cuff/EndoAnchors	0	0	0	1	0	0	1
Aortic cuff / chimney	0	0	0	0	1	0	1
Aortic cuff / stent	0	0	0	0	1	0	1[∞]
EndoAnchors	0	0	0	1	0	0	1
Secondary Intervention for Type Ib Endoleak[*]	0 0% (0/189)	0 0% (0/182)	0 0% (0/177)	0 0% (0/162)	2 1.4% (2/148)	1 0.8% (1/129)	3 1.6% (3/190)
Additional limbs placement	0	0	0	0	2	1	3
Secondary Intervention for Type II Endoleak[*]	0 0% (0/189)	1 0.5% (1/182)	0 0% (0/177)	2 1.2% (2/162)	7 4.7% (7/148)	6 (7) 4.7% (6/129)	15 (17)[€] 7.9% (15/190)
Coil or/and glue embolization	0	1	0	2	7	6	15[€]
Secondary Intervention for Type III Endoleak[*]	0 0% (0/189)	0 0% (0/182)	0 0% (0/177)	0 0% (0/162)	1 0.7% (1/148)	0 0% (0/129)	1 0.5% (1/190)
Additional limb placement	0	0	0	0	1	0	1

	1-Month	6-Month	1-Year	2-Year	3-Year	4-Year	Total
Number of Patients Eligible	189	182	177	162	148	129	
Patients with Any Intervention	1 0.5% (1/189)	5 2.7% (5/182)	8 4.5% (8/177)	7 4.3% (7/162)	12 8.1% (12/148)	8 6.2% (8/129)	34
Number of Interventions	1	5	9	9	14	9	47
Secondary Intervention for Stent graft kink*	0 0% (0/189)	0 0% (0/182)	0 0% (0/177)	0 0% (0/162)	1 0.7% (1/148)	0 0% (0/129)	1 0.5% (1/190)
Stent	0	0	0	0	1	0	1
Secondary Intervention for Other*,¥	1 0.5% (1/189)	0 0% (0/182)	0 0% (0/177)	1 0.6% (1/162)	0 0% (0/148)	0 0% (0/129)	1 (2) 0.5% (1/190)
Stent placement for vascular injury	1	0	0	0	0	0	1
Fem-stop device for vascular access site bleeding	0	0	0	1	0	0	1

* – Results through 4 year follow-up are presented as the number of patients with an event (number of events), percent of total patients at risk in the study.
β – One patient underwent a secondary intervention due to thrombus (thrombus of bilateral limbs of abdominal aortic endograft) during the 2-year window.
¥ – Other includes one secondary intervention which occurred at procedure due to a vascular injury and one secondary intervention which ccurred at 2-years due to a procedure complication (bleeding of vascular access site after the secondary intervention for the Type II endoleak).
∞ – One patient underwent a secondary intervention in the 2-year window and 3-year window for the same Type Ia endoleak, however this patient is only counted once in the total column.
± – One patient underwent a secondary intervention in the 1-year window due to the occlusion which included both the fem-fem bypass and explant of the device, however, this patient is only counted once in the total column.
€ – One patient underwent a secondary intervention in the 3-year window and 4-year window for the same Type II endoleak, however this patient is only counted once in the total column.

2.2.12 Patient Accountability and Partial 5 year Follow-Up Data

As of September 2018, one hundred fifteen (115) patients have completed their 5 year follow-up visits. Of the 115 patients, ninety-seven (97) patients had CTs completed and assessed by the Core Lab and ninety-four (94) patients had X-rays completed and assessed by the Core Lab. Study follow-up is ongoing.

Based on partial 5-year data, there were 20 aneurysm enlargements (including 18 persisting from 4 years, with 2 new identified expansions associated with Type II endoleaks), 1 persisent Type Ia endoleak from the 4 year visit, 6 new Type II endoleaks (41 persisting from the 4 year visit), and 4 secondary interventions for Type II endoleak repair (coiling/ embolization).

Between 4-year and partial 5-year follow-up, there were three patients with new stent strut fractures and three patients (with prior stent fractures) observed with additional stent strut fractures. In all, there were 20 patients with 40 transrenal stent fractures observed through (partial) 5 years:

- 13 patients having a single fracture,

- 2 patients having two fractures,
- 3 patients having three fractures,
- 1 patient having six fractures, and
- 1 patient having eight fractures (including the 2 additional fractures identified at the 5 year visit).

Among the 7 patients with more than one stent strut fracture, 5 patients were observed with additional stent strut fractures following the time point that initial fractures were first observed. All patients with stent fracture had no clinical sequelae attributable to stent fracture.

There were no additional reports of aneurysm-related mortality, additional Type Ib, Type IIIa, Type IIIb, or Type V endoleaks, device malfunctions, stent graft migration, stent graft patency related-events, or conversion to surgery beyond the 4-year follow-up.

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: gender and geographic region (U.S. vs. Japan).

3.1 Gender Analysis

There were no statistically significant differences by gender in the primary safety and effectiveness endpoints. Notable was the one incidence of aneurysm-related mortality in a female patient, compared to none in the male patients. All incidences of secondary intervention at 1-year occurred in male patients.

3.2 Country of Procedure Analysis

There are no statistically significant differences in primary safety and effectiveness by country as shown in **Table 32.**

Table 32. Primary Safety and Effectiveness Results by Country

Primary Endpoints	INCRAFT Patients			
	US (N = 134)	Japan (N = 56)	Difference 95% CI *	P-value
Primary Safety Endpoint				
MAE rate at 30 days	4.5% (6/134)	0.0% (0/56)	4.5%(-2.4%,9.4%)	0.1822
Primary Effectiveness Endpoint				
Successful Aneurysm Treatment to 1-Year †	85.6%(101/118)	92.7% (51/55)	-7.1%(-15.8%,4.1%)	0.2186

* - The 95% Confidence Intervals for Difference in Proportions are calculated using the Newcombe Score method.
† - Successful Aneurysm Treatment is described as the composite endpoint of the following:
- Absence of post-operative aneurysm enlargement (growth > 5mm) or migration (> 10mm), compared to the one month size measurement at any time up to 1-year;
- Absence of post-operative conversion to open surgery, sac rupture, endoleak Type I/III, or graft occlusion (including unilateral or bilateral limb occlusion) at any time up to 1-year;
- Considered a Technical Success as defined below.
  - Technical Success at the conclusion of the index procedure, defined as successful insertion of the delivery system through the vasculature and successful deployment of the device at the intended location. The endovascular graft must be patent, with absence of types I or III endoleaks or aneurysm sac rupture, at the time of procedure completion as confirmed by angiography or other imaging modality.

4. Pediatric Extrapolation

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

E. Financial Disclosure

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

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: no investigators
- Significant payment of other sorts: no investigators
- Proprietary interest in the product tested held by the investigator: no investigators
- Significant equity interest held by investigator in sponsor of covered study: one investigator.

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

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

A. Panel Meeting Recommendation

At an advisory meeting held on June 12, 2018, the Circulatory System Devices Panel of the Medical Devices Advisory Committee voted 11-4 that there is reasonable assurance the device is safe, 14-0 (with 1 abstention) that there is reasonable assurance that the device is effective, and 11-4 that the benefits of the device do outweigh the risks in patients who meet the criteria specified in the proposed indication.

The panel information can be found at the following link: *https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/ucm608613.htm*

B. FDA's Post-Panel Action

In addition to the final vote, panel members also made it clear during deliberations that approval of this device would only be appropriate for a limited patient population. Based on the panel discussion and because of the high rates of patency-related events, stent strut fractures, and aneurysm enlargement, FDA concluded that the indications for use should be limited to patients with complex vascular access morphology. These patients currently have limited endovascular options for aneurysm repair.

Based upon the INSPIRATION study results, the panel recommended a post approval study. FDA worked interactively with the sponsor to design an appropriate post approval study plan to monitor and communicate information regarding patient selection and expected outcomes.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The INSPIRATION study met its pre-defined primary effectiveness endpoint defined as a composite endpoint consisting of peri-procedural technical success and the absence of the following post-operatively at 1 year: aneurysm enlargement, implant migration, conversion to open surgery, aneurysm sac rupture, Type I or III endoleak, and graft occlusion.

Of 173 patients evaluated at 1 year, 152 patients had successful aneurysm treatment at 1 year after the index procedure (87.9%). Peri-procedural technical success was 94.1% (176/187). The failures to meet technical success include the device not deployed at the intended location in 2 patients and Type I endoleaks at the time of procedure

completion in 9 patients. Additionally, there were 2 conversions to open surgery, 3 Type I endoleaks, and 7 graft occlusions noted through 1 year. These events were all adjudicated by the Clinical Events Committee (CEC) to meet the definition of unsuccessful aneurysm treatment. There were no post-operative aneurysm sac enlargements, graft migration, or aneurysm sac ruptures noted through 1 year. The lower 95% confidence interval was 83%, meeting the effectiveness performance goal of 80%.

Although the pre-defined, 1-year, composite effectiveness endpoint was met, only total occlusions were included in the endpoint definition. Twelve additional patients had stenoses in their grafts through 1 year. With respect to additional 1-year outcomes, 8 patients had at least 1 fracture of the transrenal stent (14 fractures total). There was a total of 15 secondary interventions, including 2 fem-fem bypasses. The majority of secondary interventions were associated with stent graft occlusions and stenoses.

There have been no aneurysm sac ruptures reported in the study.

Patients with additional effectiveness-related events reported beyond 1 year, through 4 years, include the following:

- 5 limb migrations;
- 2 aortic bifurcate migrations of 10 mm;
- 4 Type Ia endoleaks
- 3 Type Ib endoleaks;
- 1 Type IIIb endoleak;
- 28 aneurysm expansions;
- 9 newly identified with at least one transrenal stent fracture (total of 31 fractures in 17 patients);
- 3 occlusions;
- 5 stenoses; and
- 1 kink.

There have been a total of 108 Type II endoleaks reported during the study, with the majority of new endoleaks identified through 1 year (98). Twenty-four (24) Type II endoleaks were associated with aneurysm expansion.

Secondary interventions beyond 1 year and through 4 years were conducted for the following reasons:

- 3 for stent graft occlusions (1 fem-fem bypass, 1 axillo-bifemoral bypass, 1 relining);
- 1 for stent graft stenosis or thrombosis (3 stents/thrombectomy);
- 6 for Type Ia endoleaks;
- 3 for Type Ib endoleaks (1 with limb migration);
- 16 for Type II endoleaks;
- 1 for Type IIIb endoleak:
- 1 for device kink; and

- 1 other (bleeding at suture site after intervention for Type II endoleak).

Five-year follow-up is not complete. New events for patients reported at 5 years include 2 aneurysm expansion; 6 Type II endoleak; 4 secondary interventions for Type II endoleaks; 3 new patients with at least 1 stent fracture; and 3 patients with fracture propagation.

There have been no clinical sequelae associated with the transrenal stent fractures to date. The long-term clinical relevance of the fractures is unknown. Because they are in the component of the device that may aid in securing the endovascular graft to the aorta, future potential events include migration, Type I endoleak, rupture and death, emphasizing the need for lifelong surveillance in these patients.

Although the primary composite effectiveness endpoint was met for the INSPIRATION study, a high percentage of study patients had effectiveness-related observations throughout study follow-up. Based on these observations and the panel comments, the longer-term effectiveness supports approval for a limited patient population.

B. Safety Conclusions

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

The INSPIRATION study met its pre-defined composite primary safety endpoint defined as the absence of major adverse events (MAEs) at 30-days post-procedure. There were 6 patients with 7 MAEs at the end of 30-days after the implantation procedure (6/190, 3.2%). One patient died of a myocardial infarction (MI) on the second post-operative day. There was 1 patient with a stroke, and 4 patients had blood loss of at least 1,000 cc. There were no cases of new onset of renal failure, respiratory failure, paralysis or paraparesis, or bowel ischemia. The 95% upper confidence limit of this estimate of the primary safety endpoint was 6.1%. The INSPIRATION study met its 20% safety performance goal.

MAE and the individual components at 6 months and annually through 5 years were secondary endpoints of the study. The overall rate of MAEs is 7.0% at 6 months, 10.9% at 1 year, 18.8% at 2 years, 22.8% at 3 years and 30.3% at 4 years. The overall MAE rates are primarily driven by the incidence of death, stroke, and myocardial infarction, all deemed unrelated to the INCRAFT by the Clinical Events Committee (CEC).

Additionally, device-related and procedure-related complications, through 30 days, 6 months, and annually to 5 years were secondary endpoints. The incidence of device-related SAEs was 4.8% in the first year, excluding the perioperative period. A lower rate (1.1% to 3.7%) was observed at all other intervals through 5 years, including the perioperative period. The incidence of procedure-related SAEs was 10.5% within the

first 30 days of the index procedure, and decreased following the perioperative period to an annual rate of approximately 3% or lower.

Freedom from all-cause mortality was estimated to be 99.5% at 30 days, 98.4% at 180 days, 96.8% at 1 year, 92.2% at 2 years, 87.6% at 3 years and 79.5% at 4 years. There was 1 aneurysm-related mortality, which occurred 2-days post-operatively.

The rates and types of secondary interventions and rates of stent fractures and aneurysm expansion should also be considered when evaluating the safety of the INCRAFT device. Although the rates of MAEs and serious adverse events do not raise safety concerns, the totality of the safety data only support approval for a limited patient population.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. INCRAFT's low profile and flexible delivery system offer potential benefits to patients requiring AAA repair who have limited endovascular treatment options due to complex access anatomy. In the clinical study, there were no ruptures and the only aneurysm-related death occurred 2-days post-operatively, demonstrating the benefit to patients of endovascular treatment of their aneurysms.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The MAEs reported under this study are consistent with other studies of endovascular grafts to treat AAA. Device-related risks include aneurysm expansion, stent graft occlusion, the need for secondary intervention and fracture of the transrenal stent, as described above.

Additional factors to be considered in determining probable risks and benefits for the INCRAFT device include the following:

- Untreated AAA is associated with a high risk of rupture and death once the aneurysm reaches the threshold for needing repair.
- Endovascular repair is generally associated with less procedural morbidity and mortality as compared to open surgical repair of AAA.
- Patients generally prefer endovascular to open surgical repair despite the need for life-long follow-up and the potential for needing additional interventions.
- The INSPIRATION study was not designed to compare event rates across endovascular graft studies and caution should be applied in making direct comparisons between reported rates. However, the device-related risks associated with the use of the INCRAFT are not consistent with those reported for other endovascular graft studies, supporting a limited intended patient population, that is, patients with complex access vessel morphology.
- The patients enrolled in the INSPIRATION study were not limited to those with complex vascular access morphology. However, access vessel morphology would not be expected to impact long-term outcomes and,

therefore, the benefit/risk profile based on the enrolled study patients can be extrapolated to this population that has an unmet clinical need.

In conclusion, given the available information above, the data support that for the endovascular treatment of patients with infrarenal AAA and complex vascular access morphology, the probable benefits outweigh the probable risks.

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

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The primary safety and efficacy endpoints for the study were met. Patients with limited endovascular treatment options for repair of their AAAs will benefit from use of the INCRAFT device as they will be able to avoid the morbidity and mortality associated with open surgical repair.

XIII. CDRH DECISION

CDRH issued an approval order on 11/27/2018. The final conditions of approval cited in the approval order are described below.

Cordis has agreed to provide a Clinical Update to physician users at least annually. At a minimum, this update will include, for the INSPIRATION study cohort and post-approval study cohort, respectively, a summary of the number of patients for whom data are available, with the rates of major adverse events, aneurysm-related mortality, aneurysm rupture, secondary endovascular procedures, conversions to surgical repair, endoleaks, aneurysm enlargement, prosthesis migration, occlusions, stenoses, losses of device integrity, and other procedure or device-related events. Reasons for secondary interventions and conversion to open surgery as well as causes of aneurysm-related death and rupture are to be described. Additional relevant information from commercial experience within and outside the United States is also to be included. A summary of any explant analysis findings is to be included. The clinical update for physician users and the information supporting the updates must be provided in the Annual Report.

In addition to the Annual Report requirements, Cordis has agreed to provide the following data in postapproval study (PAS) reports for each PAS listed below.

1. Long Term Follow-up Study: This is a prospective, consecutively enrolling, single-arm, multi-center study that consists of continued follow-up of all available subjects from the INSPIRATION pivotal study. A total of 190 subjects were enrolled in the study and remaining subjects will be followed for 5 years, with the exception of subjects identified with fracture(s) within the first 5 years who will be offered follow-up for an additional 5

years (total of 10 years of follow-up). Secondary endpoints through 5 years (through 10 years for patients with fracture(s)) will include all-cause mortality, aneurysm-related mortality, aneurysm rupture, secondary interventions, conversion to open surgery, losses of device integrity, device occlusions, stenosis or kink, aneurysm enlargement (> 5 mm), stent graft migration (≥ 10 mm), all types of endoleaks, and other device-related events. No formal hypothesis testing will be performed for the longer-term follow-up.

2. INCRAFT U.S. Post Approval Study: The INCRAFT U.S. Post Approval Study is a multi-center, open label, single arm, prospective post approval study. The objective of the study is to collect real-world safety and effectiveness outcomes of the INCRAFT® AAA Stent Graft System eligible for the endovascular treatment of abdominal aortic aneurysms in routine clinical practice. The study will prospectively enroll a minimum of 250 subjects at up to 40 U.S. sites. Follow-up will occur at 30 days, 1 year, and 2 years post index procedure. Patients identified with fracture(s) within the first 2 years will be followed for an additional 3 years for a total of 5 years of follow-up. The primary endpoint is successful aneurysm treatment through 2 years post procedure. Additional endpoints will be collected and reported at each follow-up point through 2 years post procedure (through 5 years for patients with stent fracture(s)), including Major Adverse Events (MAE), aneurysm enlargement (>5mm), aneurysm-related mortality, all types of endoleaks, aneurysm sac rupture, device integrity (e.g. stent strut fracture), device migration (>10 mm), graft occlusion, stenosis or kink, conversion to open surgery and secondary interventions. Procedure-related clinical utility measures will also be captured. Outcomes will be reported using descriptive statistics.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.