SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Vascular Hemostasis Device

Device Trade Name: MANTA™ Vascular Closure Device

Device Procode: MGB

Applicant's Name and Address: Essential Medical, Inc.
260 Sierra Drive, Suite 120
Exton, PA 19341 USA

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P180025

Date of FDA Notice of Approval: February 1, 2019

II. INDICATIONS FOR USE

The MANTA Vascular Closure Device is indicated for closure of femoral arterial access sites while reducing time to hemostasis following the use of 10-20F devices or sheaths (12-25F OD) in endovascular catheterization procedures.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the MANTA Vascular Closure Device labeling.

V. DEVICE DESCRIPTION

The MANTA Vascular Closure Device consists of a 14F or 18F MANTA Closure Device, a 14F or 18F Sheath with Introducer, and an 8F Depth Locator (Figure 1). The MANTA Closure Device is composed of a delivery handle containing the implantable closure unit, which consists of an absorbable collagen hemostat and an absorbable polymer anchor (also known as a toggle) that are connected by a suture. The closure unit is deployed using the depth locator, sheath, introducer and delivery handle. Hemostasis is achieved primarily by the mechanical means of the anchor-arteriotomy-collagen sandwich, which is supplemented by the coagulation-inducing properties of the collagen (Figure 2). An extra-vascular radiopaque lock secures and marks the location of the

absorbable unit for future identification on fluoroscopy. The delivery handle features a tension indicator and orientation markings to facilitate proper deployment of the absorbable unit. The MANTA Vascular Closure Device components are not made from latex rubber.

The 14F MANTA Vascular Closure Device is for access sites in the femoral artery following the use of 10-14F devices or sheaths (maximum OD of 18F).

The 18F MANTA Vascular Closure Device is for access sites in the femoral artery following the use of 15-20F devices or sheaths (maximum OD of 25F).

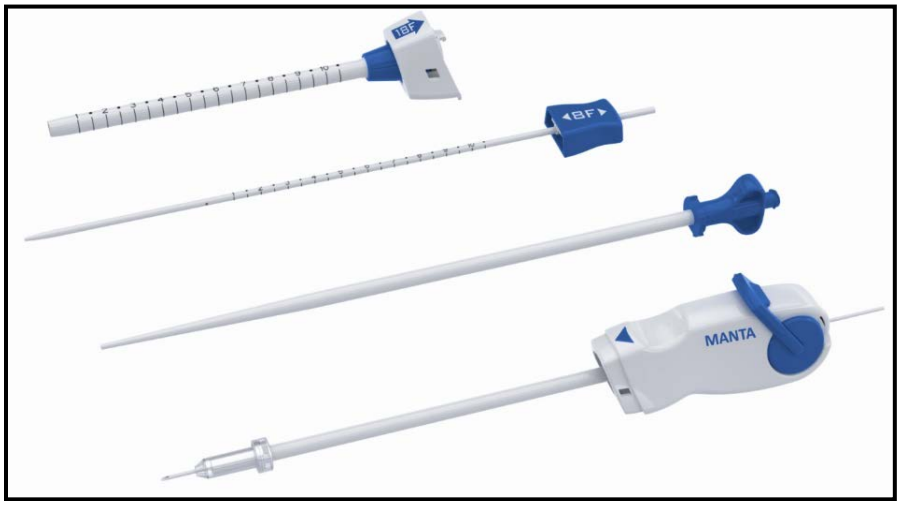

Figure 1: MANTA Closure Device Platform (18F)

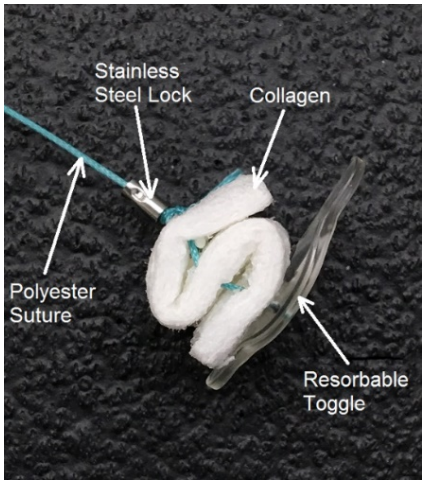

Figure 1: MANTA Closure Device Implant (18F)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for closure of femoral arteriotomies resulting from large-bore endovascular catheterization procedures. For large diameter sheaths up to 21F in size, surgical cutdown and the Perclose ProGlide® Suture Mediated Closure System provide alternatives to the subject device. For sheaths larger than 21F, the only approved alternative is surgical cutdown. 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 MANTA Vascular Closure Device received European Union CE Mark approval in July 2016 and is available for sale in the following countries: Iceland, the Netherlands, Germany, Italy, Denmark, Sweden, Finland, Norway, Switzerland, Austria UK, France, Belgium, Spain, Portugal, Luxembourg, Estonia, Latvia, Lithuania, Poland, the Czech Republic, Hungary, Slovenia, Slovakia, Croatia, Serbia, Montenegro, Macedonia, Bosnia, Bulgaria and Romania. The MANTA Vascular Closure Device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Ischemia of the leg or stenosis of the femoral artery.
- Local trauma to the femoral or iliac artery wall, such as dissection.
- Retroperitoneal bleeding as a result of access above the inguinal ligament or the most inferior border of the epigastric artery (IEA).
- Perforation of iliofemoral arteries, causing bleeding/hemorrhage.
- Thrombosis formation or embolism.
- Nerve damage or neuropathy.
- Other access site complications leading to bleeding, hematoma, pseudoaneurysm, or arterio-venous fistula, possibly requiring blood transfusion, surgical repair, and/or endovascular intervention.

Potential Adverse Events associated with any large bore intervention, including the use of the MANTA Vascular Closure Device, include but are not limited to:

- Arterial damage
- Arterio-venous fistula
- Bradycardia
- Compartment syndrome
- Death related to the procedure
- Deep vein thrombosis
- Ecchymosis
- Edema

- Infection at the puncture site which may require antibiotics or extended hospitalization
- Inflammatory response
- Late arterial bleeding
- Oozing from the puncture site
- Pressure in groin/access site region
- Vessel laceration or trauma
- Wound dehiscence

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Bench testing was performed in accordance with design verification test protocols that were developed to verify that the device meets product specifications. Testing included the following:

Table 1: Bench (Design Verification) Testing

Test	Purpose	Acceptance Criteria	Result
Device Deployment in Physiologic Model	Test a device in the physiological model and evaluate deployment-associated specifications of the MANTA.	Evaluation of deployment experience: Pass/Fail for each of various qualitative evaluation criteria	Pass
Device Deployment in Mark-10 Tensile Test Apparatus	Deploy a device in a tensile tester. The test measures various forces at different points of a MANTA deployment.	Collagen Pull Out Force: <1.75 lbF Minimum Running Force: >0.1 lbF Peak Running Force: <1.0 lbF Ultimate Device Failure: >3.17 lbF	Pass
Tube Joint Integrity and Tensile Strength	Measure the maximum tensile force that a tube can undergo before breaking, and measuring the tensile strength of a tube and component joint strength.	Tubes & hubs must withstand a minimum tensile force of 5.91 lbF Sheath hub to sheath housing must withstand a minimum tensile force of 12 lbF Lumen must withstand a minimum tensile force of 2.25 lbF	Pass
MANTA Toggle Tensile Test	Measure the tensile strength of a MANTA toggle.	Toggle must withstand a minimum tensile force of 5.91 lbF	Pass
Collagen Integrity Test	Determine collagen	Collagen must withstand a	Pass

Test	Purpose	Acceptance Criteria	Result
	tensile strength.	minimum tensile force of >15g under specific test conditions	
Hemostasis Valve Leak Test	Conduct a hemostasis valve test in accordance with ISO 11070.	Sheath hemostasis valve must not leak (pass/fail)	Pass
MANTA Lever Actuation Force	Measure the force that is required to actuate the lever.	Force required to activate <2.5 lbF	Pass
MANTA Suture Lock Corrosion Testing	Verify corrosion resistance per ISO 11070 and ASTM F2129-17.	No signs of corrosion per ISO 11070 and ASTM F2129	Pass
MRI Compatibility Testing	Confirm MRI compatibility of the stainless steel lock component of the MANTA.	Testing conducted in accordance with labeling the device as MR Conditional per ASTM 2052, ASTM 2119, ASTM 2182.	Pass
Toggle Deployment Angle Test	Measure the toggle angle after the deployment lever is actuated.	Toggle angle relative to carrier tube must be 35°-60°	Pass
Suture Tensile Test	Measure the tensile strength of a MANTA suture lock assembly	Suture lock assembly must withstand a minimum tensile force of 3.17 lbF	Pass
Bypass Tube Insertion Force Test	Measure the force required to insert the bypass tube into the sheath.	Bypass tube insertion force no greater than 10 lbF	Pass
Suture Lock Assembly Lock Sliding Force Test	Measure the sliding force of the suture locks as they slide over the suture under simulated deployment tensions.	Both suture locks must slide at acceptable force (0.1-0.5 lbF)	Pass

B. Sterilization

The MANTA Vascular Closure Device is sterilized using gamma radiation and has been validated using Method VD_{max}^{25}, in accordance with AAMI/ANSI/ISO 11137-2:2013. Results obtained from the sterilization validation show that the product satisfies a minimum Sterility Assurance Level (SAL) of 10^{-6}.

C. Biocompatibility

Biocompatibility testing was performed in accordance with ISO 10993-1:2009 and FDA guidance. The MANTA delivery handle and delivery system are classified as an external communicating device that is in contact with circulating blood for limited exposure (less than 24 hours) following the large-bore interventional procedure. The MANTA implantable unit (toggle, collagen, suture and suture lock) are classified as an implant device with blood contact for a permanent duration (greater than 30 days) that has the potential for direct

contact with circulating blood. Per ISO 10993-1, the following tests were performed on the MANTA closure unit and delivery system:

Table 2: Biocompatibility Testing

Test Article	Test Category / ISO Standard	Specific Test	Result
MANTA Closure Unit	Cytotoxicity ISO 10993-5	L929 Neutral Red Uptake (24 hr extraction)	Pass
MANTA Closure Unit	Cytotoxicity ISO 10993-5	MEM Elution (72 hr extraction)	Pass
MANTA Closure Unit	Sensitization ISO 10993-10	Kligman Maximization	Pass
MANTA Closure Unit	Intracutaneous Reactivity/Irritation ISO 10993-10	Intracutaneous Injection	Pass
MANTA Closure Unit	Acute Systemic Toxicity ISO 10993-11	Systemic Injection	Pass
MANTA Closure Unit	Acute Systemic Toxicity ISO 10993-11	Rabbit Pyrogen Test (Material Mediated)	Pass
MANTA Closure Unit	Genotoxicity ISO 10993-3	Rodent Blood Micronucleus Assay Repeat Dose	Pass
MANTA Closure Unit	Genotoxicity ISO 10993-3	Mouse Lymphoma Mutagenesis Assay	Pass
MANTA Closure Unit	Genotoxicity ISO 10993-3	*Salmonella Typhimurium* and *Escherichia Coli* Reverse Mutation Assay – with Confirmation (Ames Assay)	Pass
MANTA Closure Unit	Hemocompatibility ISO 10993-4	Hemolysis – Rabbit Blood Direct and Indirect Contact	Pass
MANTA Closure Unit	Subchronic Toxicity ISO 10993-11	ISO Subacute Intraperitoneal Toxicity Study with Histopathology, Clinical Chemistry and Hematology - 28 Day - 14 Repeat Dose - Rats	Pass
MANTA Closure Unit	Subchronic Toxicity ISO 10993-11	ISO Subchronic Intravenous Toxicity Study with Histopathology, Clinical Chemistry and Hematology - 28 Day - 28 Repeat Dose - Rats	Pass
MANTA Closure Unit	Chemical Characterization Testing ISO 10993-18	Extractable and Leachable Testing	N/A

Test Article	Test Category / ISO Standard	Specific Test	Result
MANTA Closure Unit	Chemical Characterization Testing ISO 10993-18	Exhaustive Extractables Chemical Characterization Testing	N/A
MANTA Delivery System	Cytotoxicity ISO 10993-5	ISO MEM Elution Using L929 Mouse Fibroblast Cells	Pass
MANTA Delivery System	Sensitization ISO 10993-10	ISO Guinea Pig Maximization Sensitization Test	Pass
MANTA Delivery System	Intracutaneous Reactivity/Irritation ISO 10993-10	ISO Intracutaneous Irritation Test	Pass
MANTA Delivery System	Acute Systemic Toxicity ISO 10993-11	ISO Acute Systemic Injection Test	Pass
MANTA Delivery System	Acute Systemic Toxicity ISO 10993-11	ISO Materials Mediated Rabbit Pyrogen Test	Pass
MANTA Delivery System	Hemocompatibility ISO 10993-4	ASTM Hemolysis – Direct Contact and Extract Method	Pass
MANTA Delivery System	Hemocompatibility ISO 10993-4	Complement Activation C3a and SC5b-9 Assay	Pass
MANTA Delivery System	Hemocompatibility ISO 10993-4	Thrombogenicity Study in Sheep ISO3	Pass

All tests were successfully completed and all acceptance criteria were met for the delivery handle, delivery system and implant unit. In conclusion, the biocompatibility testing performed on the MANTA device demonstrated that the biocompatibility requirements of ISO 10993-1 have been met.

D. Packaging Testing

The MANTA device packaging was evaluated in accordance with ISO 11607-1:2006. Testing included 18-month real-time aging, testing of physical distribution environmental stresses, including testing for environmental conditioning, shock, vibration and compression hazards; evaluation of package strength using physical strength methods; and validation testing of package sterility using physical integrity detection, applying the appropriate standards. The device passed the packaging simulations and confirmed the sterile barrier integrity and minimum seal strength for the MANTA device packaging per the standard test methods. Following the shipping simulations, it was confirmed that the MANTA device meets the performance specifications.

E. Shelf-life Testing

The MANTA device was evaluated to support a shelf life of 18 months. Devices were real time aged at ambient temperature for 18 months. The testing demonstrated that devices that were aged for 18 months met the functional, visual, and performance

requirements. No anomalies related to aging were found during testing. Based upon the testing, the MANTA device is labeled with an 18-month shelf life.

F. Animal Studies

A series of acute and chronic animal studies were performed to characterize the safety and performance of the MANTA Vascular Closure Device. The open laparotomy porcine aorta model had previously been identified as an appropriate cardiovascular surrogate for the human patient and was the model used. Studies were conducted to evaluate the functionality of the delivery device, as well as the vascular and physiologic responses to the implantable closure unit. GLP survival studies evaluated the implant through 300 days post-deployment. The data demonstrate that the MANTA implantable closure unit is well tolerated and is fully encapsulated by the body within approximately 180 days. The implant is completely resorbed in approximately 1 year, except for the radiopaque lock and the suture. The following table provides a summary of the design validation animal studies.

Table 3: Design Validation Animal Studies using MANTA Device and Delivery System

Study Number	Implant Date	Endpoints	# Devices/ Animals	# animals/ time point	Key Findings
RXY00011	Oct 2014	30, 90, 180 days	9/3	1@30 days, 1@90 days, 1@180 days	Toggle security and early encapsulation with progressive capsular response to 180-days
RXY00012	Jan 2015	240, 300 days	6/2	1@240 days, 1@300 days	Toggle security and early encapsulation with progressive capsular response
RXY00013	Jan 2015	Acute	7/1	1	Acceptable performance characteristics of 14F MANTA device.
RXY00014	Feb 2016	180 days	6/2	2@180 days	Toggle security and early encapsulation with progressive capsular response to 180-day. Absence of particulate emboli, thromboemboli, inflammation, necrosis, ischemia or infarction with zero scores for downstream coronary band/planar site evaluation.

G. Polymer Characterization and Degradation Studies

In addition to the chemical characterization testing listed in Table 2, the polymer used to mold the MANTA toggle was independently tested for composition and impurities. The

testing confirmed there are no unexpected chemicals, monomers or other impurities detected within the polymer, confirming the suitability of the material for the MANTA Vascular Closure Device.

The MANTA polymer degradation and resorption process was studied through the animal studies listed in Table 3. An in-vitro study was conducted to mechanically and chemically map the degradation process of the MANTA polymer. An In Vitro/ In Vivo correlation is in development to confirm that the polymer degrades in an expected and controlled manner, that it maintains adequate strength through the encapsulation period, and that it is completely degraded within a clinically relevant timeframe.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish reasonable assurance of safety and effectiveness of vascular closure with the MANTA device following large-bore percutaneous interventions at investigational sites in the US and Canada under IDE G160115. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Enrollment in the study was initiated on November 28, 2016 with the first roll-in subject; the first Primary Analysis Cohort (PAC) subject was enrolled on December 12, 2016. PAC enrollment was completed on September 26, 2017, and the last PAC subject completed follow-up on December 5, 2017. The database for this PMA reflected data collected through December 5, 2017, which was the complete dataset, and included 263 Primary Analysis Cohort subjects. In addition, 78 roll-in (training) subjects were enrolled. There were 20 investigational sites, 19 in the US and one in Canada.

The study was a multicenter, prospective, single-arm clinical study. The study was designed to evaluate the safety and effectiveness of the MANTA device in closing large-bore femoral arterial access sites in comparison to performance goals (PGs) for the primary safety and effectiveness endpoints. The study population was defined as subjects undergoing cardiac or peripheral large-bore interventional procedures, such as transcatheter aortic valve implantation (TAVI) or endovascular aneurysm repair (EVAR), via the femoral artery approach when using a sheath or device of 12-25F OD. The PG for the primary safety endpoint was based on published data from the use of suture-mediated closure devices for access site closure in patients undergoing TAVI or EVAR and on expert clinical advisor input. The PG for the primary effectiveness endpoint was based on published data from the use of suture-mediated closure devices or surgery for access site closure in patients undergoing TAVI or EVAR. A clinical acceptance criterion (CAC) was established for the secondary safety endpoint and was based on expert clinical advisor input.

An independent Clinical Events Committee (CEC) was responsible for systematic review and adjudication of MANTA site/leg related Major Complications, Minor Complications

or VARC-2 Major Vascular Complications. A core lab was used to independently evaluate all ultrasound images. An independent Data and Safety Monitoring Committee (DSMC) reviewed aggregated data from the study at two timepoints during study enrollment.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the MANTA pivotal study was limited to patients who met the following pre-operative inclusion criteria:

   1. Candidate for elective or planned (i.e., not emergent or urgent) percutaneous transcatheter interventional procedure via a 10-18F size retrograde common femoral artery approach (i.e., transcatheter aortic valve implantation [TAVI], endovascular aneurysm repair [EVAR], Impella® use)
   2. Vessel size would allow for access for the MANTA as determined by baseline CTA: minimum vessel diameter 5mm for the 14F MANTA and 6mm for the 18F MANTA
   3. Eligible for sheath removal in the catheterization lab
   4. Age $\geq$ 21 years
   5. Understand and sign the study specific written informed consent form
   6. Able and willing to fulfill the follow-up requirements
   7. In the investigator's opinion, patient is suitable for the MANTA vascular closure device, conventional hemostasis techniques and participation in an investigational trial

   Patients were not permitted to enroll in the MANTA pivotal study if they met any of the following exclusion criteria:

   1. Known to be pregnant or lactating
   2. Immunocompromised or with pre-existing autoimmune disease
   3. Systemic infection or a local infection at or near the access site
   4. Significant anemia (hemoglobin < 10 g/dL, hematocrit < 30%)
   5. Morbidly obese or cachectic (BMI > 40 kg/m^2 or < 20 kg/m^2)
   6. Known bleeding disorder including thrombocytopenia (platelet count < 100,000 cells/UL), thrombasthenia, hemophilia, or von Willebrand disease
   7. Allergy to bovine materials or any other device material, including collagen and/or collagen products, polyglycolic or polylactic acid, stainless steel or nickel
   8. Femoral artery puncture in target groin within the prior 14 days, recent femoral artery puncture in target groin that has not healed appropriately, and/or prior vascular closure device placement in target common femoral artery that the investigator determines may interfere with the MANTA device
   9. Common femoral artery with calcium, as determined by baseline CTA, precluding safe access in the opinion of the investigator or severe peripheral

vascular disease as evidenced by severe claudication when ambulating < 100 feet, weak or absent pulses in the affected limb, or ABI < 0.5 at rest
10. Previous iliofemoral intervention in region of access site, including but not limited to prior atherectomy, stenting, surgical or grafting procedures in the access area
11. Patients who have undergone use of an intra-aortic balloon pump through the arterial access site within 30 days prior to the baseline evaluation
12. Undergoing therapeutic thrombolysis
13. Patients in whom continuous oral anticoagulation therapy cannot be stopped for the peri-procedural period or patients with INR > 1.8 at the time of the procedure
14. Patient unable to be adequately anti-coagulated for the procedure
15. Patients who are not mobile and are confined to a wheelchair or bed
16. ST-elevation MI within 30 days prior to procedure or acute coronary syndrome (i.e., unstable angina or myocardial infarction) ≤ 48 hours before the catheterization procedure
17. NYHA class IV heart failure
18. Left ventricular ejection fraction < 20%
19. Unilateral or bilateral lower extremity amputation
20. Renal insufficiency (serum creatinine > 2.5 mg/dl) or on dialysis therapy
21. Existing nerve damage in the ipsilateral leg
22. Further planned endovascular procedure within the next 30 days
23. Patients who have already participated in the IDE study
24. Currently participating in another clinical trial of an unapproved investigational device or drug that has not concluded the follow-up period
25. Patient cannot adhere to or complete the investigational protocol for any reason including but not limited to geographical residence, psychiatric condition or life-threatening disease
26. Common femoral artery < 5 mm in diameter for the 14F MANTA or < 6 mm in diameter for the 18F MANTA, common femoral artery stenosis resulting in a vessel diameter < 5mm in diameter for the 14F MANTA or < 6 mm in diameter for the 18F MANTA, or > 50% diameter femoral or iliac artery stenosis

During the procedure, patients were <u>not</u> permitted to enroll in the MANTA pivotal study if they met any of the following intra-operative exclusion criteria:

27. Puncture site in the profunda femoris artery, superficial femoral artery, or at the bifurcation of these arteries
28. Common femoral artery suspected to have experienced a back wall puncture or underwent > one (1) <u>arterial</u> puncture during the catheterization procedure
29. Difficult dilation from initial femoral artery access (e.g., damaging or kinking dilators) while step dilating up to the large-bore device
30. Presence of ipsilateral femoral venous sheath

31. Puncture site located above the most inferior border of the epigastric artery (IEA) and/or above the inguinal ligament based upon bony landmarks
32. Marked tortuosity of femoral or iliac artery
33. Patient did not receive any antiplatelet or anticoagulant medications before or during the endovascular interventional procedure
34. ACT > 250 seconds prior to removal of the sheath or interventional device
35. Systolic blood pressure > 180 mmHg or diastolic blood pressure > 110 mm Hg, unless systolic or diastolic pressure can be lowered by pharmacological agents prior to closure
36. Antegrade puncture during the index procedure
37. Interventional sheath or device in place > 6 hours
38. Possible bacterial contamination of the procedure sheath or surrounding tissues during the procedure
39. Intra-procedural complication(s) at the femoral access site pre-sheath removal including: 1. Bleeding or swelling around the large bore sheath that may indicate hematoma formation and/or pseudoaneurysm formation; and 2. Peri-procedural angiographic evidence of thrombus formation or significant injury in the aorta or iliac vessels associated with procedural large bore sheath placement and/or sub-optimal anticoagulation
40. Systolic blood pressure < 90 mm Hg just prior to planned vascular closure
41. Procedure sheath or interventional device > 25F outer diameter required during the procedure

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 ± 7 days and 60 ± 14 days post-procedure. All subjects underwent non-invasive Duplex ultrasound (DUS) imaging following MANTA deployment prior to hospital discharge (within 48 hours post-procedure) and again at the 30-day follow-up visit. DUS was to be repeated at the 60-day follow-up if there were abnormal findings at 30 days. DUS was used to evaluate all related arteries and veins for patency, and the absence or presence of pseudoaneurysm, hematoma, vessel injury, vessel thrombus/thrombosis and/or iatrogenic arteriovenous communication post placement of the MANTA device. B-mode gray-scale and color Doppler images, as well as spectral Doppler waveforms for velocity measurements, were used for this purpose.

Preoperatively, a medical history was obtained including a record of the subject's demographic (i.e., age, race, ethnicity, sex) and baseline information (i.e., height, weight, labs). A baseline (within 180 days prior to consent) Computed Tomography Angiography (CTA) scan of the aorta, iliac and common femoral vessels was required to measure vessel size and assess potential access sites for disease and calcium deposits, and various laboratory tests were performed. Subjects were evaluated against the inclusion/exclusion criteria. During the dilation steps at the beginning of the interventional procedure, the MANTA depth locator was used to measure the depth of the artery; this result was noted in the

subject's record. At the end of the endovascular procedure, the access site was assessed to verify the intra-procedure eligibility criteria. The MANTA device was then deployed, and time to hemostasis was recorded. Postoperatively, the objective parameters measured during the study included any access site-related events, events occurring in the ipsilateral leg or systemic events that could be MANTA device related. Adverse events and complications were recorded at all visits.

The following table summarizes the schedule of assessments following MANTA deployment:

Table 4: MANTA U.S. Pivotal Study Schedule of Assessments

Assessment/Interval	**Post-MANTA Closure Procedure**	**Hospital Discharge**	**30D & 60D Follow-Up**[1]
Clinical Exam			X
Medication Use		X	X
ABI (Ankle- Brachial Index)	X	X	X
Duplex Ultrasound		X[2]	X[3]
Femoral Angiography	X		
Target Femoral Access Site External Visual Assessment	X	X	X
Time to Hemostasis	X		
Time to Ambulation		X	
Adverse Events	X	X	X

1. 30- day follow-up window is ± 7 days; 60- day follow-up window is ± 14 days.
2. Ultrasound performed no later than 48 hours post-MANTA deployment, if discharge is delayed. In addition, any suspected hematoma, pseudoaneurysm or AV fistula at the MANTA site was to be confirmed with ultrasound.
3. Duplex ultrasound performed at 60-day visit if there were abnormal ultrasound findings at 30-day visit.

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

3. Clinical Endpoints

The primary safety endpoint was the rate of Major Complications within 30 days following the interventional procedure. The secondary safety endpoints were the rate of Minor Complications within 30 days following the procedure and the rate of VARC-2 Major Vascular Complications within 30 days following the procedure.

Major Complications was a composite endpoint of the following:

- Vascular injury attributable to the MANTA device requiring surgical repair or stent-graft;

- Access site-related bleeding that is attributable to failure of or sub-optimal performance of the MANTA device and that results in transfusion;
- New onset ipsilateral lower extremity ischemia that originates with the common femoral artery, is attributable to the MANTA device, causes a threat to the viability of the limb, and requires surgical repair or additional percutaneous intervention;
- Access site-related nerve injury attributable to the MANTA device that is permanent (lasting > 30 days) or requires surgical repair; and
- Access site-related infection requiring intravenous antibiotics and/or extended hospitalization.

Minor Complications was a composite endpoint of the following:

- Non-treated pseudoaneurysm attributable to the MANTA device and documented by ultrasound;
- Non-treated or treated arteriovenous (AV) fistula attributable to the MANTA device and documented by ultrasound;
- Pseudoaneurysm treated with ultrasound-guided compression, ultrasound-guided thrombin injection or ultrasound-guided fibrin adhesive injection;
- Access site hematoma that is attributable to failure of or sub-optimal performance of the MANTA device, is ≥ 10 cm and is confirmed by ultrasound;
- Late (following hospital discharge) access site-related bleeding;
- Ipsilateral lower extremity arterial emboli attributable to the MANTA device;
- Ipsilateral vein thrombosis attributable to the MANTA device;
- Transient access site-related nerve injury;
- Access site wound dehiscence; and
- Localized access site infection treated with intramuscular or oral antibiotics.

VARC-2 Major Vascular Complications was a composite endpoint, adapted from Kappetein et al, of the following:

- Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure leading to death, life threatening or major bleeding [1], visceral ischemia, or neurological impairment OR
- Distal embolization (noncerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage OR
- The use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischemia or neurological impairment OR

- Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram OR
- Surgery for access site-related nerve injury OR
- Permanent access site-related nerve injury

The primary effectiveness endpoint was time to hemostasis (TTH). The secondary effectiveness endpoints were technical success, ambulation success, time to ambulation (TTA), treatment success and procedure time.

Following are the definitions of the effectiveness endpoints:

Time to Hemostasis: The elapsed time between MANTA deployment (withdrawal of sheath from artery) and first observed and confirmed arterial hemostasis (no or minimal subcutaneous oozing and the absence of expanding or developing hematoma).

Technical Success: A subject will be considered a Technical Success if percutaneous vascular closure is obtained with the MANTA device without the use of unplanned endovascular or surgical intervention.

Ambulation Success: A subject will be considered an Ambulation Success if he/she is able to ambulate for at least 20 feet/6 meters without re-bleeding.

Time to Ambulation: The elapsed time between MANTA deployment (withdrawal of sheath from artery) and when ambulation is achieved (subject standing and walking at least 20 feet/6 meters without re-bleeding).

Treatment Success: A subject will be considered a Treatment Success if he/she has Time to Hemostasis ≤ 10 minutes and has no Major Complications (as defined above).

Procedure Time: Defined as elapsed time from initial skin break (first needle insertion) to time when the post-deployment angiogram is completed.

B. Accountability of PMA Cohort

At the time of database lock, of 263 primary analysis cohort patients enrolled in the PMA study, 244 (92.8%) total patients completed the 30- day (±7 days) follow-up visit, 236 (89.7%) total patients completed the 60-day (±14 days) follow-up visit, and 228 (86.7%) patients completed both the 30-day and 60-day follow-up visits. Below is an accountability table of the Primary Analysis Cohort (PAC; roll-in subjects not shown).

Table 5: Accountability of Primary Analysis Cohort

Disposition	Totals (number vs. %)

Disposition	Totals (number vs. %)	
Number completed 30-day follow-up (primary endpoints) (30 days)/enrolled	244/263	92.8%
Number completed 60-day follow-up	236/263	89.7%
Number completed both 30-day and 60-day follow-up	228/263	86.7%
Inclusion/Exclusion violation	6	2.3%
Early Termination (through 60 days)	27	10.3%
Adverse event	0	0
Investigator decision	0	0
Lost to follow-up	4	1.5%
Withdrew consent	17	6.6%
Device explantation	1	0.4%
Death (from any cause)	5	1.9%

C. Study Population Demographics and Baseline Parameters

1. Demographics and Baseline Parameters

The demographics of the study population are typical for a VCD study performed in the US. Of the 263 enrolled subjects, 53 (20.2%) underwent EVAR procedures and 210 (79.8%) underwent TAVI procedures. No Impella VAD subjects were enrolled. The mean age was 79.4 ± 8.4 years. The percentage of male subjects was 64.6% and the mean BMI was 28.2 kg/m^2.

Table 6: Demographics (PAC)

		EVAR (N=53)	TAVI (N=210)	All Subjects (N=263)
Gender (n (%))	Female	12 (22.6%)	81 (38.6%)	93 (35.4%)
	Male	41 (77.4%)	129 (61.4%)	170 (64.6%)
Age [years]	Mean (SD)	74.9 (8.9)	80.6 (7.9)	79.4 (8.4)
Age Category	< 65	4 (7.5%)	5 (2.4%)	9 (3.4%)
	65-79	34 (64.2%)	85 (40.5%)	119 (45.2%)
	80+	15 (28.3%)	120 (57.1%)	135 (51.3%)
Race (n (%))	Asian	3 (5.7%)	4 (1.9%)	7 (2.7%)
	Black or African American	2 (3.8%)	6 (2.9%)	8 (3.0%)
	Other	0 (0.0%)	1 (0.5%)	1 (0.4%)
	White	48 (90.6%)	199 (94.8%)	247 (93.9%)
Ethnicity (n (%))	Hispanic Or Latino	5 (9.4%)	11 (5.2%)	16 (6.1%)
	Not Hispanic Or Latino	48 (90.6%)	199 (94.8%)	247 (93.9%)
Height (cm)	N	53	210	263
	Mean (SD)	173.6 (10.3)	170 (10.1)	170.7 (10.2)
	Median	173	170.2	171
	Minimum, Maximum	152, 195.6	142.2, 193	142.2, 195.6

		EVAR (N=53)	TAVI (N=210)	All Subjects (N=263)
Weight (kg)	N	53	210	263
	Mean (SD)	87 (18)	82.9 (16.3)	83.8 (16.7)
	Median	86.6	80.65	81.6
	Minimum, Maximum	56.7, 121.6	45.4, 131.2	45.4, 131.2
BMI [kg/m^2]	N	53	210	263
	Mean (SD)	28.7 (4.8)	28.6 (4.3)	28.6 (4.4)
	Median	28.5	28.1	28.2
	Minimum, Maximum	20.2, 39.9	19.9, 39.6	19.9, 39.9

2. Medical History

The PAC study population had prior cardiovascular surgical history that consisted of percutaneous coronary intervention (PCI - 85 subjects, 32.3%), coronary artery bypass graft (CABG - 50 subjects, 19%), pacemaker/implantable cardioverter defibrillator (Pacemaker/ICD - 42 subjects, 16%) and prior structural heart intervention (31 subjects, 11.8%). There were other surgical histories noted that included neuorvascular intervention (14 subjects, 5.3%), peripheral interventions (11 subjects, 4.2%) and prior aneurysm repair (seven subjects, 2.7%). Additionally, there were 132 subjects (50.2%) who had other types of surgical interventions noted in their medical history.

Table 7: Medical History (PAC)

	Statistic	EVAR (N=53)	TAVI (N=210)	All Subjects (N=263)
Prior Surgical History Events				
Aneurysm Repair	n (%)	7 (13.2)	0 (0)	7 (2.7)
CABG	n (%)	9 (17)	41 (19.5)	50 (19)
Neurovascular Intervention	n (%)	6 (11.3)	8 (3.8)	14 (5.3)
PCI	n (%)	11 (20.8)	74 (35.2)	85 (32.3)
Pacemaker/ICD	n (%)	4 (7.5)	38 (18.1)	42 (16)
Peripheral Interventions	n (%)	5 (9.4)	6 (2.9)	11 (4.2)
Structural Heart Intervention	n (%)	1 (1.9)	30 (14.3)	31 (11.8)
Other Medical History Event	n (%)	25 (47.2)	107 (51)	132 (50.2)

3. Pre-Procedural Data

Table 8 below shows the key pre-procedural data for the PAC population. Of note is that 16.0% of the PAC patients had some level of peripheral artery disease (PAD) based on baseline ankle-brachial index (ABI) of ≥ 0.5 and < 0.9, which indicates mild to moderate PAD. Patients with ABI < 0.5, which indicates severe PAD, were excluded from the study.

Table 8: Pre-Procedural Data (PAC)

		EVAR (N=53)	TAVI (N-210)	All Subjects (N=263)
Ankle-Brachial Index (n (%))	< 0.5 [1]	0…(0%)	0…(0%)	0…(0%)
	≥ 0.5 to < 0.9 [2]	9 (17.0%)	33 (15.7%)	42 (16.0%)
	≥ 0.9	43 (81.1%)	175 (83.3%)	218 (82.9%)
	Missing	1 (1.9%)	2 (1.0%)	3 (1.1)%
MANTA Device Size	14F	37 (69.8%)	5 (2.4%)	42 (16.0%)
	18F	16 (30.2%)	205 (97.6%)	221 (84.0%)
Effective Puncture Size (F)	17	36 (67.9%)	0 (0%)	36 (13.7%)
	18	0 (0%)	5 (2.4%)	5 (1.9%)
	18.6	1 (1.9%)	0 (0%)	1 (0.4%)
	21	15 (28.3%)	23 (11.0%)	38 (14.4%)
	22.5	1 (1.9%)	2 (1.0%)	3 (1.1%)
	23	0 (0%)	127 (60.5%)	127 (48.3%)
	24.5	0 (0%)	53 (25.2%)	53 (20.2%)
	Mean	18.3	23	22.1
	Median	17	23	23
Target Common Femoral Artery	Right	29 (54.7%)	151 (71.9%)	180 (68.4%)
	Left	24 (45.3%)	59 (28.1%)	83 (31.6%)
Target Common Femoral Artery Diameter (mm)	Mean (SD)	8.7 (1.8)	7.7 (1.2)	7.9 (1.4)
Sheath to Femoral Artery Ratio[3]	Mean (SD)	0.7(0.1)	1(0.2)	1(0.2)
Pre-Deployment Systolic Blood Pressure (mm Hg)	Mean (SD)	135.3 (22.6)	127.2 (20.3)	128.8 (21)
Pre-Deployment Diastolic Blood Pressure (mm Hg)	Mean (SD)	71.7 (12)	57 (11.4)	59.9 (12.9)
Pre-Deployment Activated Clotting Time (seconds)	Mean (SD)	185.6 (39.1)	174.7 (41.3)	176.9 (41)

[1] Indicates severe PAD
[2] Indicates mild to moderate PAD
[3] Defined as the sheath size outer diameter in millimeters divided by the baseline common femoral artery diameter in millimeters as determined by CT angiography

4. Anticoagulant and Antiplatelet Medications

The concomitant medications at baseline and during the procedure for the PAC population are shown below. The majority of subjects were taking aspirin at baseline (65%), and approximately one-fourth were on an anti-platelet drug at baseline (e.g., 25.9% on clopidogrel). All subjects were given heparin as part of their procedural medications.

Table 9: Baseline and Procedural Medications (PAC)

Time Point Medication Started	Anticoagulant or Antiplatelet Drug	Statistic	EVAR (N=53)	TAVI (N=210)	All Subjects (N=263)
Baseline	Apixaban	n (%)	0 (0)	12 (5.7)	12 (4.6)
	Aspirin	n (%)	38 (71.7)	133 (63.3)	171 (65)
	Clopidogrel	n (%)	15 (28.3)	53 (25.2)	68 (25.9)
	Dabigatran	n (%)	0 (0)	4 (1.9)	4 (1.5)
	Enoxaparin Sodium	n (%)	0 (0)	2 (1)	2 (0.8)
	Heparin	n (%)	0 (0)	2 (1)	2 (0.8)
	Prasugrel	n (%)	2 (3.8)	0 (0)	2 (0.8)
	Rivaroxaban	n (%)	1 (1.9)	5 (2.4)	6 (2.3)
	Ticagrelor	n (%)	0 (0)	3 (1.4)	3 (1.1)
	Warfarin	n (%)	4 (7.5)	11 (5.2)	15 (5.7)
Procedural Medication	Aspirin	n (%)	0 (0)	6 (2.9)	6 (2.3)
	Bivalirudin	n (%)	1 (1.9)	0 (0)	1 (0.4)
	Clopidogrel	n (%)	3 (5.7)	8 (3.8)	11 (4.2)
	Heparin*	n (%)	53 (100)	210 (100)	263 (100)
	Rivaroxaban	n (%)	0 (0)	1 (0.5)	1 (0.4)

* Unfractionated intravenous heparin

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the primary analysis cohort of 263 patients/procedures. The key safety outcomes for this study are presented below in **Table10**. Adverse effects are reported in **Tables 10** to**14**.

The primary safety endpoint of Major Complications within 30 days of procedure, is presented in **Table 10**. Note that all safety analyses are based on a per-subject analysis; thus, subjects with more than one event are counted only once in each analysis. The overall Major Complication rate within 30 days in the Primary Analysis Cohort was 5.3% (14/263). The exact one-sided 97.5% upper confidence bound is 8.8%, which compares favorably to the performance goal of 19.9% (**Table 11**). A Kaplan-Meier analysis of Major Complications was also performed. The results of the Kaplan-Meier analysis were identical to the simple proportion (5.3% Major Complications with a 97.5% upper confidence bound of 8.8%). In addition, the p-value for the comparison of the Major Complication rate to the performance goal was < 0.0001. Therefore, the null hypothesis was rejected, and the study met the primary safety endpoint. Additional details of the Major Complications are presented in **Table 14**.

Table 10: Major Complications

Major Complication Type	N=263	
Subjects with Any Major Complications within 30 days of procedure	**14** [1]	**5.3%**

Major Complication Type	N=263

[1] The 14 patients had 15 major complication events.

Table 11. Major Complications Compared to Performance Goal (PG)

Cohort	Observed Major Complication Rate	97.5% Upper Confidence Bound[1]	P-value (2-sided)
Overall SES Population	5.3% (14/263)	8.8%	< .0001
TAVI Subjects	6.2% (13/210)	10.4%	< .0001
EVAR Subjects	1.9% (1/53)	10.1%	0.0010

[1] Performance goal (PG) for rate of Major Complications = 19.9%

The secondary safety endpoints of Minor Complications and VARC-2 Major Vascular Complications within 30 days of the procedure are presented in **Tables 12** and **13**. The overall Minor Complication rate within 30 days was 2.7% (7/263) in the PAC population.Minor Complications is a per-subject analysis. The overall VARC-2 Major Vascular Complication rate within 30 days was 4.2% (11/263), which includes 12 events. Note that the VARC-2 Major Vascular Complications definition significantly overlaps with the definition for Major Complications; the two definitions and events are not mutually exclusive. Therefore, all the events that were classified as a VARC-2 Major Vascular Complication are also classified as a Major Complication. Three subjects had events that were adjudicated as a Major Complication but that did not count as a VARC-2 Major Vascular Complication; these were access site related major bleeding events which did not meet the VARC-2 complication definition. Per the study protocol, the Minor Complication rate was qualitatively compared to the Clinical Acceptance Criterion (CAC) established for this endpoint, which was 20%. The Minor Complication rate of 2.7% was well below the 20% CAC for Minor Complications; thus, the study met this secondary safety endpoint.

Table 12: Minor Complications

Minor Complication Type	N=263	
Subjects with Any Minor Complications within 30 days of procedure	**7** [1]	**2.7%**
Access site hematoma that is attributable to failure of or sub-optimal performance of the MANTA device, is ≥10 cm and is confirmed by ultrasound	0	0%
Access site wound dehiscence	0	0%
Ipsilateral lower extremity arterial emboli attributable to the MANTA device	0	0%
Ipsilateral vein thrombosis attributable to the MANTA device	0	0%
Late (following hospital discharge) access site-related bleeding	0	0%
Localized access site infection treated with intramuscular or oral antibiotics	0	0%

Minor Complication Type	N=263	
Non-treated or treated arteriovenous (AV) fistula attributable to the MANTA device and documented by ultrasound	0	0%
Non-treated pseudoaneurysm attributable to the MANTA device and documented by ultrasound;	3	1.1%
Pseudoaneurysm treated with ultrasound-guided compression, ultrasound-guided thrombin injection or ultrasound-guided fibrin adhesive injection.	3	1.1%
Transient access site-related nerve injury	1	0.4%

[1] The 7 patients had 8 minor complication events.

Table 13: VARC-2 Major Vascular Complications

VARC-2 Major Vascular Complication Type	N=263	
Subjects with Any VARC-2 Major Vascular Complications within 30 days of procedure	**11**	**4.2%**
Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life threatening or major bleeding,* visceral ischemia, or neurological impairment	10	3.8%
Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram	7	2.7%
Distal embolization (noncerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage	0	0%
Permanent access site-related nerve injury	0	0%
Surgery for access site-related nerve injury	0	0%
The use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischemia or neurological impairment	10	3.8%

Adverse effects that occurred in the PMA clinical study:

Major complications through 30 days as adjudicated by the Clinical Events Committee (CEC) are presented in **Table 14**. Fourteen (14) major complications were reported within 30 days: five (5) access site-related bleeding, nine (9) new onset ipsilateral lower extremity ischemia, and one (1) vascular injury.

Table 14. Summary of CEC Adjudicated Major Complications

Major Complication Type	N=263	
Subjects with Any Major Complications within 30 days of procedure	**14** [1]	**5.3%**
Access site-related bleeding that is attributable to failure of or sub-optimal performance of the MANTA device and that results in transfusion	5	1.9%
Access site-related infection requiring intravenous antibiotics and/or extended hospitalization	0	0%
Access site-related nerve injury attributable to the MANTA device that is permanent (lasting > 30 days) or requires surgical repair	0	0%
New onset ipsilateral lower extremity ischemia that originates with the common femoral artery, is attributable to the MANTA device, causes a threat to the viability of the limb, and requires surgical repair or additional percutaneous intervention	9	3.4%

Major Complication Type	N=263	
Vascular injury attributable to the MANTA device requiring surgical repair or stent-graft	1	0.4%

[1] The 14 patients had 15 major complication events.

Except in two cases, the observations that were noted during the follow-up ultrasound examinations of the study patients were minor adverse findings that are expected with large-bore interventional procedures like TAVI and EVAR which the study patients underwent. Two subjects had peri-procedural stenosis due to partial or complete intra-arterial device deployment, were adjudicated as having a major complication and had residual stenosis diagnosed on ultrasound, which was not a new finding. Other than these two major complications, the other ultrasound findings did not meet the criteria for the minor complications constituting the secondary safety endpoint, were asymptomatic, and/or were not noted by the study investigators.

2. Effectiveness Results

The analysis of effectiveness was based on time to hemostasis (TTH) in the 263 evaluable patients and is presented in **Table 15**.

The mean TTH was 1.09 ± 2.63 minutes, with a range of 0.07–17.92 minutes. The median TTH was 0.4 minute, or 24 seconds. The one-sided upper 97.5% confidence bound was 1.41 minutes, which compares favorably to the performance goal of 10 minutes (**Table 16**). In addition, the p-value for the comparison of TTH to the performance goal was < 0.0001. The null hypothesis was thus rejected, and the study met its primary effectiveness endpoint.

Table 15: Time to Hemostasis (PAC)

Endpoint	Statistic	All Subjects	One-Sided Upper 97.5% Confidence Bound
Time to Hemostasis (minutes)	N	263	
	Mean (SD)	1.09 (2.63)	1.41
	Median	0.4	
	Minimum, Maximum	0.07, 17.92	

Table 16: Time to Hemostasis Compared to Performance Goal (PG)

Cohort	Observed Hemostasis Time (Minutes, mean)	97.5% Upper Confidence Bound[1]	P-value (2-sided)
Overall PAC Population	1.09 ± 2.63	1.41	< .0001

TAVI Subjects (N=210)	1.22 ± 2.83	1.60	< .0001
EVAR Subjects (N=53)	0.58 ± 1.52	1.00	< .0001

[1] Performance goal (PG) for Time to Hemostasis = < 10 minutes

The vast majority of PAC subjects experienced a TTH of < 1 minute, as illustrated in **Figure 3** and **Table 17**, and only a small number of subjects had a TTH > 5 minutes (N=15).

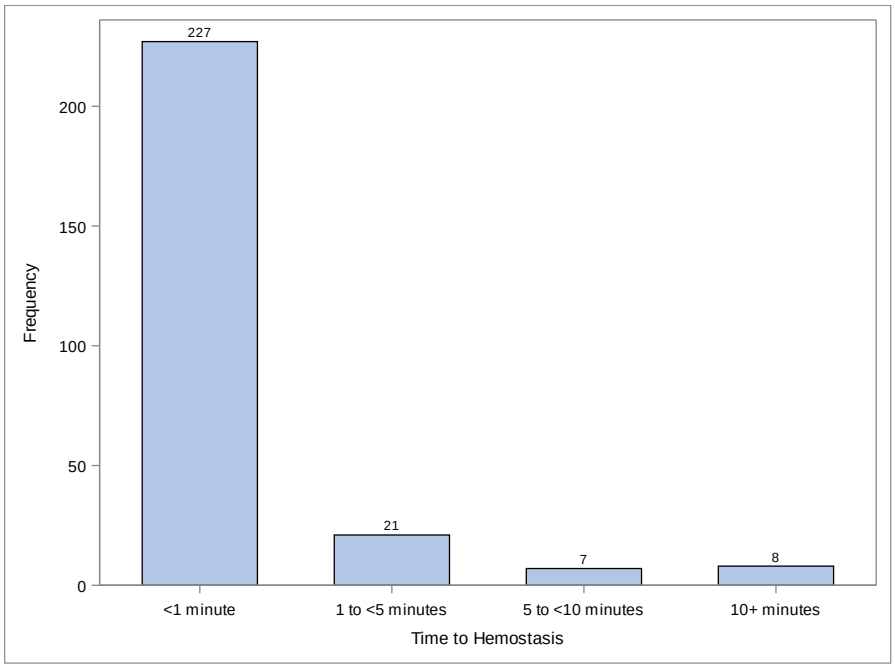

Figure 2: Distribution of Time to Hemostasis (PAC)

Table 17: Time to Hemostasis by Time-Point (PAC)

Analysis Dataset	**PAC**	
Time to Hemostasis	**Frequency (N=263)**	**Percent**
< 1 minute	227	86.3%
1 to < 5 minutes	21	8.0%
5 to < 10 minutes	7	2.7%
10+ minutes	8	3.0%

Secondary effectiveness endpoints as defined in the protocol included Ambulation Success, Technical Success, and Treatment Success following treatment with the MANTA device. In the PAC population, 255 (97%) subjects met the criteria for Ambulation Success, 257 (97.7%) subjects met the criteria for Technical Success, and 246 (93.5%) subjects met the criteria for Treatment Success (**Table 18**).

Table 18: Secondary Effectiveness Endpoints (PAC)

Endpoint	All Subjects n (%)
Ambulation Success Able to ambulate for at least 20 feet/6 meters without re-bleeding	255 (97.0)
Technical Success Percutaneous vascular closure is obtained with the MANTA device without the use of unplanned endovascular or surgical intervention	257 (97.7)
Treatment Success Time to Hemostasis ≤ 10 minutes and has no Major Complications	246 (93.5)

Time to Ambulation (TTA) was a secondary effectiveness endpoint that was measured for informational purposes only. In the PAC population, the median TTA was 16.87 hours; mean TTA was 22.02 ± 25.63 hours, with a large range of 4.13-236.05 hours, reflecting the complexity of some subjects' post-procedure course. Similarly, Procedure Time was a secondary effectiveness endpoint that was measured for informational purposes only. In the PAC population, the median procedure time was 74.72 minutes with a mean of 79.91 ± 39.23 (range 28-309.78 minutes). Informational secondary effectiveness endpoints are illustrated in **Tables 19** and **20**.

Table 19: Time to Ambulation and Procedure Time

Endpoint	All Subjects n (%)
Time to Ambulation (hours)	
Mean (SD)	22.02 (25.63)
Median	16.87
Minimum, Maximum	4.13, 236.05
Procedure Time (minutes)	
Mean (SD)	79.91 (39.23)
Median	74.72
Minimum, Maximum	28, 309.78

Table 20: Time to Ambulation by Time-Point (PAC)

Analysis Dataset	PAC	
Time to Ambulation	**Frequency (N=263)**	**Percent**
< 6 hours	25	9.5%
6 to < 12 hours	68	25.9%
12 to < 24 hours	103	39.2%
1 to < 2 days	48	18.3%
2 to < 4 days	14	5.3%

Analysis Dataset	PAC	
Time to Ambulation	Frequency (N=263)	Percent
4+ days	5	1.9%

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with effectiveness outcomes: gender, race, ethnicity, age, procedure type, MANTA device size, index device type (manufacturer/brand interventional device, e.g., Edwards Sapien, Gore AAA Excluder), effective puncture size, and sheath to femoral artery ratio. There was no statistically significant difference in the time to hemostasis for gender, race, ethnicity, age, procedure type and index device type. There was a statistically significant difference in time to hemostasis for MANTA device size and sheath to femoral artery ratio; 14F MANTA devices had shorter TTH than 18F devices, and subjects with a larger SFAR (sheath to femoral artery ratio, sheath larger than the artery) had a longer TTH than those with smaller SFAR.

There was a statistically significant difference for safety outcomes for gender and age. Major Complications, Minor Complications and VARC-2 Major Vascular Complications occurred more frequently in female subjects and in the elderly (> 80 years) than in male and younger subjects.

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 42 investigators of which none were full-time or part-time employees of the sponsor and one 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: 0
- Significant payment of other sorts: 0
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The assessment of effectiveness for the MANTA Vascular Closure device was based on mean time to hemostasis (TTH) in the PAC population. On average, hemostasis was achieved in 1.09 ± 2.63 minutes, which compares favorably to the performance goal of 10 minutes. Therefore, the study met its primary effectiveness endpoint. Median TTH was 0.4 minute, and only 15 of 263 subjects had a TTH > 5 minutes. This duration compares favorably to other marketed vascular closure devices.

Hemostasis was achieved by the MANTA device alone without the need for adjunctive methods in 90.9% of subjects. 9.1% of subjects required manual/mechanical compression, and two subjects required a contralateral balloon inflation. In addition, 84.4% did not require treatment for oozing. In the PAC population, 97.0% of subjects met the criteria for Ambulation Success, 97.7% met the criteria for Technical Success, and 93.5% met the criteria for Treatment Success. In covariate analysis, TTH was associated with MANTA device size and SFAR. TTH was not affected by age, gender or race/ethnicity.

B. Safety Conclusions

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

The safety assessments for the MANTA Vascular Closure device were based on the primary endpoint of the rate of Major Complications within 30 days in the primary analysis cohort, and the secondary endpoints of the rate of Minor Complications and the rate of VARC-2 Major Vascular Complications within 30 days. The analysis provided to support this PMA suggests that the device met the primary endpoint Peformance Goal of 19.9% with an observed Major Complication rate of 5.3%, with an exact one-sided 97.5% upper confidence bound of 8.8%. Additionaly, the analysis provided suggests that the device met the secondary endpoint Clinical Acceptance

Criterion of 20% with an observed Minor Complication rate of 2.7%. The rate of VARC-2 Major Vascular Complications within 30 days, which is by definition a subset of Major Complications, was 4.2%. All 11 subjects adjudicated as having a VARC-2 Major Vascular Complication, were also adjudicated as having had a Major Complication. There was no PG or CAC for this secondary endpoint. All Major Complications occurred on or before the subject's discharge date; there were no Major Complications that occurred after the discharge date. In covariate analysis, Major Complications, Minor Complications and VARC-2 Major Vascular Complications occurred more frequently in female subjects and in the elderly (> 80 years) than in male and younger subjects.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The potential benefits of using the MANTA Vascular Closure Device for closure of large-bore arterial access sites is that the treatment allows for: hemostasis to be achieved in around one minute for a majority of subjects (1.09 minutes), a technical success rate of 97.7%, and a treatment success rate of 93.5%. The device performance is associated with acceptable major complications rate through 30 days of 5.3%.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Risks associated with the device include major access site-related bleeding, access site-related infection requiring hospitalization, access site-related nerve injury, new onset of lower extremity ischemia, and vascular injury which may occur up to 30 days. Additional risks include minor access site hematoma, access site wound dehiscence, lower extremity arterial emboli, ipsilateral vein thrombosis, late access site-related bleeding, localized access site infections, arteriovenous fistulas, pseudoaneurysms, and nerve injury, which may occur up to 30 days. The expected rates for the aforementioned major and minor access-site complications are 5.3% and 2.7%, respectively.

1. Patient Perspectives

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

In conclusion, given the available information above, the data support that for the percutaneous closure of femoral artery access sites in interventional patients utilizing 12-25F OD procedural sheaths/devices, the probable benefits outweigh the probable risks.

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. As

discussed above the benefits of potential reduced time to hemostasis coupled with low rates of access-site complications suggest that the benefits of using the MANTA Vascular Closure Device outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on February 1, 2019. The final conditions of approval cited in the approval order are described below.

Within 12 months of PMA approval, the applicant should submit a non-clinical post-approval study report with *in vivo* study results for the 33, 48, and 57-week time-points for your ongoing in vivo degradation study. The results should include evaluation of mass loss, inherent viscosity and molecular weight at each time point. The results of the 33, 48, and 57-week time-points should be submitted in one PMA report, accompanied with updated In-Vitro/In-Vivo Correlation (IVIVC) information. If any of the results indicate that the toggle is not fully degraded *in vivo*, the applicant should provide rationale for why any remaining toggle components do not raise a clinical safety concern.

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.

XV. REFERENCES

[1] Kappetein AP, Head SJ, Généreux P et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: The Valve Academic Research Consortium-2 consensus document. J Thorac Cardiovasc Surg 2013;145:6-23.