

# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

Device Generic Name:	Percutaneous cardiac ablation catheter for treatment of atrial fibrillation with irreversible electroporation
Device Trade Name:	VARIPULSE™ Platform (VARIPULSE™ Catheter; TRUPULSE™ Generator; Sterile Interface Cable; nGEN™ Pump)
Device Procode:	QZI
Applicant's Name and Address:	Biosense Webster, Inc. 31 Technology Drive, Suite 200 Irvine, CA, USA 92618
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P240006
Date of FDA Notice of Approval:	November 06, 2024

## II. INDICATIONS FOR USE

### **VARIPULSE Catheter**

The VARIPULSE Catheter is indicated for use in catheter based cardiac electrophysiological mapping (stimulating and recording) and, when used with a TRUPULSE™ Generator, for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation. The catheter provides location information when used with the CARTO™ 3 System. The device is intended for adults 22 years old and above.

### **TRUPULSE Generator**

The generator is indicated for use in conjunction with compatible cardiac ablation catheter to deliver pulsed field (PF) ablation during cardiac ablation procedures.

### **Sterile Interface Cable**

This cable provides a means to connect a Biosense Webster electrophysiology catheter to the appropriate equipment. The cable may be reused subject to the cleaning and sterilization restrictions detailed in Instructions for Use.

## **nGEN Pump**

The nGEN Pump is a peristaltic pump designed to work with a compatible irrigation tubing set, either independently or with a compatible generator, to deliver irrigation solution to compatible irrigated catheter.

### **III. CONTRAINDICATIONS**

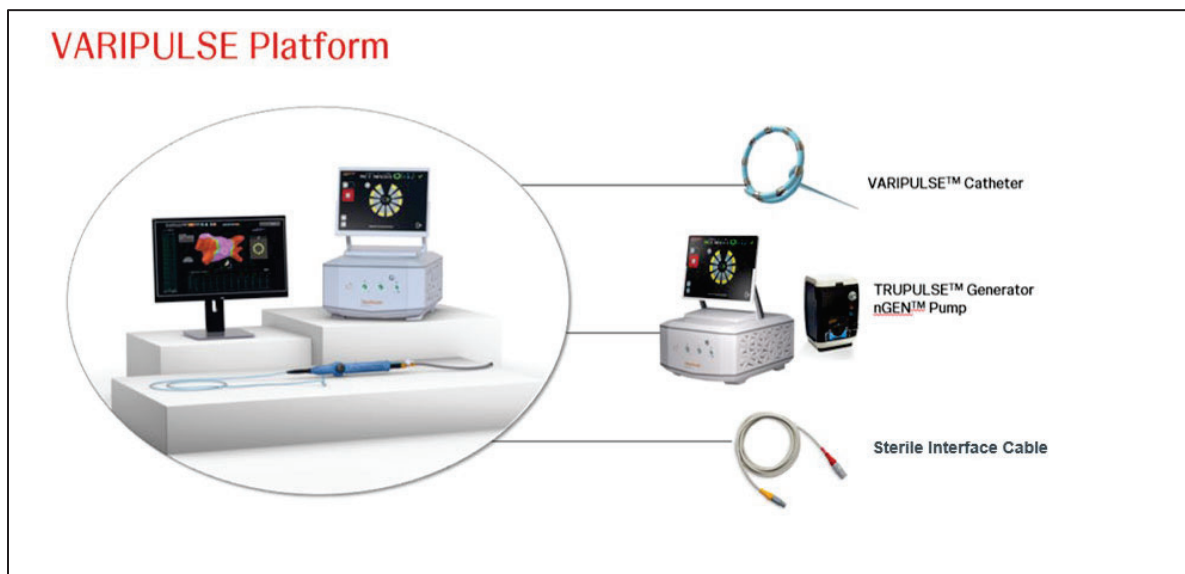
1. Do not use the catheter if the patient has had an atriotomy within the preceding eight weeks. Recent surgery may increase the risk of perforation.
2. Do not use the catheter in a patient with a myxoma or an intracardiac thrombus. Doing so may precipitate emboli.
3. Do not use the catheter in a patient with a prosthetic valve. Doing so may damage the prosthetic valve, result in device entrapment or embolization of device components.
4. Do not use the catheter in the coronary arterial vasculature. Doing so may damage the coronary arterial vasculature or cause an infarction.
5. Do not use the catheter in a patient with an active systemic infection. Doing so may increase the risk of cardiac infection.
6. Do not use the catheter via the transseptal approach in a patient with an interatrial baffle or patch. The opening may persist and produce an iatrogenic atrial shunt.
7. Do not use the catheter via the retrograde trans aortic approach. Doing so may increase the risk of perforation.
8. Do not use the catheter in the ventricles. The catheter may become tangled with the valves.
9. Do not use the catheter in a patient with a recent history of myocardial infarction. The patient may be susceptible to ventricular tachycardia.
10. Do not use the catheter in a pregnant woman. The effects of pulse field energy on a fetus are unknown.
11. Do not use the catheter in arterial or jugular access sites. Doing so may cause injury to the vasculature and may increase incidents of hematoma.

#### IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the VARIPULSE Platform labeling.

#### V. DEVICE DESCRIPTION

The VARIPULSE Platform (VARIPULSE Catheter; TRUPULSE Generator; Sterile Interface Cable; nGEN Pump) includes the following components:



**Figure 1: VARIPULSE Platform**

#### VARIPULSE Catheter

The VARIPULSE Catheter (the catheter) is a steerable, multi electrode, irrigated, pulsed field ablation catheter. Attached to the distal end of the shaft is a bidirectional deflectable segment. Attached to the segment is a circular tip containing 10 ring electrodes. The usable length of the catheter is 115 cm.

The catheter was designed to facilitate cardiac electrophysiological mapping (stimulating and recording) and ablation. The catheter was also designed to be used with the TRUPULSE Generator (the generator) to transmit biphasic high voltage pulses to the electrodes on the catheter to perform ablation.

The circular tip of the catheter is a loop that can be expanded and contracted to accommodate the anatomy of the left atrium. The uncontracted loop diameter is  $34 \pm 1$  mm and the contracted loop diameter is  $\leq 25$  mm at room temperature with further contraction expected during clinical use due to body temperature. The 10 electrodes on the loop are perforated with a series of holes to facilitate irrigation of the ablation area. The electrodes are made from noble metals and may be used for visualization, stimulation, recording, and ablation.

A standard Luer fitting is attached to the lumen that extends from the handle of the catheter. Heparinized normal saline is injected through the port in the Luer fitting. During mapping and ablation, the saline passes through the internal lumen of the catheter and through the holes of the electrodes. An irrigation pump controls the irrigation flow.

In the loop of the catheter are 3 single axis sensors (SAS) which transmit location information to the CARTO™ 3 System for catheter visualization. Refer to the instructions for use for the CARTO 3 System for information on using the catheter for mapping procedures.

The catheter is provided sterile (ethylene oxide (EO)) and is intended for single use only.

### TRUPULSE Generator

The generator is intended for use with the catheter to deliver pulsed field energy to cardiac tissue. The generator includes the following components:

- Console
- Monitor
- Remote Monitor (optional)
- Foot Pedal
- Cables

The generator delivers high-voltage, high-frequency pulses of short duration to the electrodes located around the distal loop of the catheter. The generator connects to the catheter through the Sterile Interface Cable and interfaces with the nGEN Pump, CARTO 3 System, electrophysiology (EP) recording system, and EP stimulator.

Through the generator user interface, the user can select ablation modes (e.g., choose electrodes), monitor ablation output (e.g., number of applications), and view system messages, among other functions.

### Sterile Interface Cable

The Sterile Interface Cable provides a means for connecting the catheter to the generator. The Sterile Interface Cable is provided sterile (EO) and can undergo hospital-based reprocessing and sterilization using EO or steam (up to 20 cycles).

### nGEN Pump

The nGEN Pump (the pump) is a peristaltic irrigation pump designed to deliver heparinized saline through sterile tubing to the standard Luer fitting on the catheter.

## **VI. ALTERNATIVE PRACTICES AND PROCEDURES**

There are several other alternatives for the correction of symptomatic, drug refractory, recurrent, persistent atrial fibrillation. 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.

- Treatment with medicines that help control the rate and/or rhythm of the heart and other medicines that reduce the likelihood of clots forming (known as medical or pharmacologic therapy).
- Cardioversion to restore the heart's normal rhythm (with electrical shock or medicine).
- Implantable devices that control the rate of the heart.
- Implantable devices that reduce the likelihood of clots forming.
- Catheter ablation with other devices approved in the United States.

## **VII. MARKETING HISTORY**

The VARIPULSE Platform is approved in Japan and the European Union. The device is not currently marketed in any region. The device has not been withdrawn from marketing for any reason, including those 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.

- Acute Respiratory Distress Syndrome (ARDS)
- Air embolism
- Allergic reaction
- Anemia
- Anesthesia reaction
- Arrhythmias
- Atelectasis
- Atrio-Esophageal Fistula
- Atypical flutter
- AV fistula
- Cardiac perforation/tamponade
- Cardiac Thromboembolism
- Cerebrovascular accident (CVA)
- Chest pain/discomfort
- Complete heart block, temporary or permanent

- Component damage to ICD or implantable pacemaker
- Congestive heart failure
- Coronary artery dissection
- Coronary artery spasm
- Death
- Dislodgement of ICD or permanent pacing leads
- Endocarditis
- Exacerbation of pre-existing atrial fibrillation, or other arrhythmia
- Expressive aphasia
- Hair loss due to anesthesia
- Heart failure
- Hematuria
- Hemorrhage
- Hemothorax
- Hypertension/Hypotension
- Increase in frequency or duration of episodes of typical atrial flutter
- Increased phosphokinase level
- Infection, localized or systemic
- Injury to skin, muscle, connective tissue due to body position, electrical cardioversion, etc.
- Laceration
- Leakage of air or blood into the lungs or other organs due to perforation
- Local hematoma/ecchymosis
- Mobile strands in the inferior vena cava
- Myocardial infarction
- Obstruction or perforation or damage to the vascular system
- Pericardial effusion/tamponade
- Pericarditis
- Phrenic nerve damage
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism
- Renal failure
- Respiratory depression/failure
- Retroperitoneal hematoma
- Rhabdomyolysis, including that produced by body position or propofol
- Seizure
- Shortness of Breath
- Skin burns due to cardioversion, tape, etc.
- Syncope/Dizziness

- Temperature elevation
- Thromboembolism
- Transient ischemic attack (TIA)
- Unintended complete/incomplete AV, sinus node or other heart block or damage
- Urinary tract injury or infection related to the urinary catheter
- Valvular damage/insufficiency
- Vasovagal reactions
- Volume overload
- Worsening obstructive, restrictive, or other form of pulmonary disease
- X-ray radiation injury of skin, muscle and/or organ

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

## **IX. SUMMARY OF NON-CLINICAL STUDIES**

For non-clinical testing, a risk-assessment based testing program was used to validate the VARIPULSE Platform. Catheter designs were evaluated per guidance documents and recognized consensus standards to confirm the necessary verification/validation activities. Ablation in the porcine model was determined to be the method of choice to validate the VARIPULSE System. Bench studies evaluated mechanical and electrical performance, and material safety (biocompatibility).

### **A. Laboratory Studies**

#### ***Design Verification***

##### **VARIPULSE Catheter**

Design verification testing was performed to verify the performance and mechanical integrity of the catheter. A risk-based assessment was used to identify appropriate tests, test methods, and sample sizes. All devices undergoing design verification were subjected to 3x EO sterilization, accelerated aging (1 year), and distribution simulation. This can be seen in Table 1 below.

**Table 1: Design Verification Testing (VARIPULSE Catheter)**

Test Name	Description	Result
Visual Inspection, Deflection, and Contraction	To identify manufacturing defects or anomalies caused by preconditioning.	Pass
Electrical	To evaluate DC lead resistance of each ring electrode circuit and isolation of the ring electrodes.	Pass
Irrigation Flow Rate	To evaluate the flow characteristics of the catheter.	Pass
Loop Buckle Force	To quantify the force required to buckle the loop lumen.	Pass
Tip Stiffness	To evaluate the force required to pull the catheter when it is deflected.	Pass
Side Force	To quantify the side force generated by a deflected rotated catheter tip.	Pass
Catheter Soak	To simulate clinical usage.	Pass
Steering through Vascular Model	To evaluate catheter integrity during sheath insertions.	Pass
In-Bath Rotation and Deflection	To evaluate catheter integrity during manipulation.	Pass
Handle to Shaft Flexion Fatigue	To evaluate flexural reliability.	Pass
Catheter Initialization Check	To verify recognition on the CARTO 3 System.	Pass
Ablation Cycling	To evaluate catheter integrity following simulated ablation cycles.	Pass
Irrigation Flow Rate	To evaluate flow characteristics.	Pass
DC Resistance	To evaluate DC lead resistance of each ring electrode circuit and isolation of the ring electrodes.	Pass
Visual Inspection, Deflection, and Contraction	To identify manufacturing defects or anomalies caused by postconditioning.	Pass
Torque Test of Entire Catheter	To evaluate catheter integrity during rotation.	Pass
Tensile Test of Loop to Housing	To quantify the tensile strength required to break the full length of a catheter.	Pass
Tensile Test of Transition Joint of Soft Tip to Shaft	To quantify the tensile strength required to break the full length of a catheter.	Pass
Tensile Test of Transition Joint of Shaft to Handle	To quantify the tensile strength required to break the full length of a catheter.	Pass
Sidearm/Luer Hub Torque Test	To evaluate the torque resistance of the irrigation side arm.	Pass
Sidearm/ Luer Hub Pull Test	To evaluate the tensile strength of the irrigation side arm.	Pass

### Sterile Interface Cable

Based on the similarities between the CARTO 3 cable assembly and the Sterile Interface Cable assembly, testing performed for the CARTO 3 cable assembly was applied to the Sterile Interface Cable assembly, including the 3 year shelf life (product and packaging), 3x EO sterilization cycles (product and packaging), 20x EO

reuse/re-sterilization cycles (product), and 20x autoclave reuse/re-sterilization cycles (product).

The cables were subjected to integrity and performance testing specified in the approved protocol and design verification showed to meet functionality requirements with regards to safety, maintain sufficient mechanical integrity after preconditioning and simulated clinical use, and maintain performance as expected throughout simulated clinical use. The Sterile Interface Cable samples were subjected to 3x EO. 20 sterilization and twenty pulsed field ablation cycles. Cable testing conducted is shown in Table 2 below.

**Table 2: Design Verification Testing (Sterile Interface Cable)**

Test Name	Description	Result
Electrical Test, DC Resistance and Leakage	To evaluate the DC lead resistance of each wire and the shields, and confirms the resistance between wires.	Pass
Tensile Strength of the Trunk Cable Material	To confirm the tensile strength of the cable trunk	Pass
Visual Inspection	To confirm suitability of samples for test.	Pass
Flex Life	To confirm durability in anticipated use.	Pass

### TRUPULSE Generator

Testing of the TRUPULSE Generator included system-level testing, software and cybersecurity testing, and testing for conformance with FDA-recognized voluntary consensus standards for basic safety and essential performance. A list of voluntary consensus standards used to support the safety and effectiveness of the VARIPULSE Platform, including the TRUPULSE Generator, is available at the end of this section.

### ***Biocompatibility***

Biocompatibility testing was performed on the VARIPULSE Catheter. Device design, materials, construction, and manufacturing environment were evaluated. All biocompatibility testing of the VARIPULSE Catheter met the ISO 10993-1 biocompatibility testing requirements for external communicating devices with circulating blood for limited contact time ( $\leq 24$  hours).

### ***Sterilization***

#### VARIPULSE Catheter

The VARIPULSE Catheter is EO sterilized using an all-in-one process, where preconditioning, sterilization and aeration take place in the same chamber. All sterilization validations were executed per ISO 11135:2014. The sterility assurance level (SAL) has been verified to meet the minimum requirement of  $10^{-6}$ . All EO and

ethylene chlorohydrin (ECH) residual levels were found to be within the allowable limits per ISO 10993-7 for limited exposure devices.

Detailed assessments confirmed that the VARIPULSE Catheter could be adopted into designated validated sterilization cycles at specified contract sterilizers.

These adoption assessments included an evaluation of device packaging, construction, materials, manufacturing environments, and design (e.g., lumen size for gas penetration). Based on these assessments, the VARIPULSE Catheter does not provide a greater sterilization challenge when sterilized using the validated Biosense Webster EO sterilization cycles.

### Sterile Interface Cable

The Sterile Interface Cable is EO sterilized and certified as sterilized to a Sterility Assurance Level (SAL) of 10<sup>-6</sup> in compliance with ISO 11135:2014. An assessment was performed to determine if the Sterile Interface Cable could be adopted into the previously validated standard BWI sterilization cycles. A comparison of the design, manufacturing, packaging, and sterilization of the Sterile Interface (D-1337-01-S) to the CARTO™ 3 System Interface Cable (D-1286-XX-S) supported adoption of Sterile Interface Cable into previously validated BWI sterilization cycles. The Interface Cable may be re-sterilized up to 20 maximum number of cycles. Validated cleaning and sterilization process, and relevant cleaning and validation restrictions are provided in the Instruction for Use.

### *Shelf Life*

#### VARIPULSE Catheter

Catheter integrity and performance testing was conducted after 3x EO sterilization, 1-year accelerated aging, and distribution stimulation conditioning. The results support a 1-year shelf life.

#### TRUPULSE Generator

The various components (monitor, a console, and a cable kit) of the TRUPULSE Generator are non-sterile and are packaged within a Pelican box. Packaging validation was performed for the packaging designed for the system and for the monitor and console. Transportation conditions are defined in the labels and the instructions for use.

### Sterile Interface Cable

Based on the similarities between the CARTO 3 cable assembly and the Sterile Interface Cable assembly, testing performed for the CARTO 3 cable assembly was

applied to the Sterile Interface Cable assembly, including the 3-year shelf life (product and packaging).

### nGEN Pump

The nGEN Pump was previously approved under a bundled PMA supplement (P950005/S084, P990025/S069, P010068/S069, P030031/S127, and P040036/S089).

### ***Voluntary Consensus Standards***

The VARIPULSE Platform demonstrated conformity with the following FDA-recognized and non-recognized voluntary consensus standards.

- ISO 10993-1:2020
- ISO 10993-4:2014
- ISO 10993-4:2017
- ISO 10993-5:2009
- ISO 10993-7:2008
- ISO 10993-10:2023
- ISO 10993-11:2017
- ISO 10993-12:2021
- ISO 10993-18:2020
- ISO 10993-23:2021
- ISO 11135:2014
- ISO 11138-2:2017
- ISO 11737- 1:2018/A1:2021
- ISO 11737-2:2020
- ISO 11607-1:2020/A11:2022
- EN ISO 11607-2:2020/A11: 2022
- ISO 14644-1:2015
- ISO 14644-2:2015
- IEC 60601-1 Edition 3.2 2020-08
- IEC 60601-1-2 Edition 4.1 2020-09
- IEC 60601-2-2 Edition 6.0 2017-03
- IEC 60601-1-6 Edition 3.2 2020-07
- IEC 62304 Edition 1.1 2015-06
- ISO 14971 Third Edition 2019-12
- ISO 15223-1 Fourth Edition 2021-07
- IEC 62366-1 Edition 1.1 2020-06
- ISO 20417 First Edition 2021-04

## **B. Animal Studies**

Two chronic animal studies were conducted to validate the performance of the VARIPULSE Catheter interfacing with compatible mapping system, the TRUPULSE Generator, and the Sterile Interface Cable. Testing performed under these protocols were Good Laboratory Practice (GLP)-compliant in accordance with 21 CFR Part 58.

The objective of the GLP studies was to demonstrate the overall safety of the VARIPULSE Catheter when ablating at clinically relevant anatomical locations, including the pulmonary veins, when used with the TRUPULSE Generator, 8.5 F sheath, compatible mapping system, nGEN Pump, Sterile Interface Cable, an EP recording system, and standard pacing system in a chronic beating heart model.

The studies demonstrated that the TRUPULSE Generator, when used with the VARIPULSE Catheter, performs as intended when ablating per recommendations within the instructions for use.

Additionally, two acute animal studies were conducted to evaluate the volume and count of microbubbles produced with the VARIPULSE Catheter during simulated cardiac ablation procedures in a porcine model. The VARIPULSE generated microbubbles were similar in size to bubbles generated by radiofrequency (RF) ablation and did not suggest an increased risk of thromboembolism during application of PF energy.

## **X. SUMMARY OF PRIMARY CLINICAL STUDY**

The applicant performed a clinical study titled, “Assessment of Safety and Effectiveness in Treatment Management of Atrial Fibrillation with the BWI IRE Ablation System,” (AdmIRE, ClinicalTrials.gov Registration: NCT05293639) to establish a reasonable assurance of safety and effectiveness of percutaneous catheter ablation with the VARIPULSE Platform for the treatment of symptomatic, drug refractory, recurrent paroxysmal atrial fibrillation in the US under IDE G220034. Data from this clinical study were the basis for the PMA approval decision. Data from the outside US (OUS) study titled, “A Study for Treatment of Paroxysmal Atrial Fibrillation (PAF) by Pulsed Field Ablation (PFA) System With Irreversible Electroporation (IRE),” (InspIRE) were used to support the safety of the VARIPULSE Platform (specifically, the occurrence of neurological events including asymptomatic cerebral embolism/lesions and pulmonary vein (PV) stenosis).

### **A. Study Design**

The AdmIRE study was a prospective, non-randomized, multicenter, clinical investigation conducted at 33 investigational sites in the US. A total of 384 subjects were enrolled in the Pilot Phase (22 subjects) and Pivotal Phase (362 subjects). The Pivotal Phase consisted of the roll-in and main phase. The first 1-2 subjects for each ablating physician using the VARIPULSE platform were prospectively assigned as

roll-in subjects to verify consistent workflow for study device components and to minimize any learning curve effects.

A pre-specified endpoint analysis was conducted to evaluate effectiveness between days 91-365 after the index procedure. The study database was locked on December 19, 2023.

#### 1. Clinical Inclusion and Exclusion Criteria

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

1. Symptomatic paroxysmal atrial fibrillation (AF) with:
  - a. At least two symptomatic AF episodes within the last six months from enrollment.
  - b. At least one AF episode electrocardiographically documented within 12 months prior to enrollment. Electrocardiographic documentation could include, but not be limited to, ECG, transtelephonic monitoring (TTM), Holter monitor or telemetry strip.
  - c. A physician's note indicating recurrent self-terminating AF within 7 days.
2. Failed at least one antiarrhythmic drug (AAD) (Class I or Class III) as evidence by recurrent symptomatic AF, intolerable side effects to the AAD, or contraindication to the AAD.
3. Age 18-75 years.
4. Willing and capable of providing consent.
5. Able and willing to comply with all pre-, post-, and follow-up testing and requirements.

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

1. Previously diagnosed with persistent AF (> 7 days in duration).
2. AF secondary to electrolyte imbalance, thyroid disease, or reversible or noncardiac cause (e.g., untreated documented obstructive sleep apnea and acute alcohol toxicity).

3. Previous surgical or catheter ablation for AF.
4. Patients known to require ablation outside the PV region (e.g., atrioventricular reentrant tachycardia, atrioventricular nodal reentry tachycardia, atrial tachycardia, ventricular tachycardia and Wolff-Parkinson-White).
5. Documented severe dilatation of the LA (LAD >50mm) antero-posterior diameter on imaging within 6 months prior to enrollment.
6. Documented LA thrombus by imaging within 48 hours of the procedure.
7. Documented severely compromised LVEF (LVEF <40%) by imaging within 6 months prior to enrollment.
8. Uncontrolled heart failure or New York Heart Association (NYHA) Class III or IV.
9. History of blood clotting, bleeding abnormalities or contraindication to anticoagulation (heparin, warfarin, or dabigatran).
10. Documented thromboembolic event (including TIA) within the past 12 months.
11. Previous PCI/MI within the past 2 months.
12. Coronary Artery Bypass Grafting (CABG) surgery within the past 6 months (180 days).
13. Valvular cardiac surgical/percutaneous procedure (i.e., ventriculotomy, atriotomy, valve repair or replacement and presence of a prosthetic valve).
14. Unstable angina within 6 months.
15. Anticipated cardiac transplantation, cardiac surgery, or other major surgery within the next 12 months.
16. Significant pulmonary disease (e.g., restrictive pulmonary disease, constrictive or chronic obstructive pulmonary disease) or any other disease or malfunction of the lungs or respiratory system that produces severe chronic symptoms.
17. Significant congenital anomaly or medical problem that in the opinion of the investigator would preclude enrollment in this study.
18. Prior diagnosis of PV stenosis.

19. Pre-existing hemi diaphragmatic paralysis.
  20. Acute illness, active systemic infection, or sepsis.
  21. Presence of intracardiac thrombus, myxoma, tumor, interatrial baffle or patch or other abnormality that precludes catheter introduction or manipulation.
  22. Severe mitral regurgitation (Regurgitant volume  $\geq$  60 mL/beat, Regurgitant fraction  $\geq$  50%, and/or Effective regurgitant orifice area  $\geq$  0.40cm<sup>2</sup>).
  23. Presence of implanted pacemaker or Implantable Cardioverter-Defibrillator (ICD) or other implanted metal cardiac device that may interfere with the IRE energy field.
  24. Presence of a condition that precludes vascular access (such as IVC filter).
  25. Current enrollment in an investigational study evaluating another device or drug.
  26. Women who are pregnant (as evidenced by pregnancy test if premenopausal), lactating, or who are of child-bearing age and plan on becoming pregnant during the course of the clinical investigation.
  27. Life expectancy less than 12 months.
  28. Presenting contra-indications for the devices used in the study, as indicated in the respective Instructions for Use (IFU).
2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at discharge, 7 days, 1 month, 3 months, 6 months, and 12 months, with examinations listed in Table 3.

**Table 3: Follow-Up Schedule**

	Pre-Procedure	Ablation / Discharge		Phone / Virtual	Follow-Up Visits				
	Screening/Baseline	Study Ablation (Day 0)	Discharge	7 Days (Day 7-10)	1 Month (Day 23-37)	3 Month (Day 76-104)	6 Month (Day 150-210)	12 Month (Day 335-395)	Unscheduled
Visit Number	1	2	3	4	5	6	7	8	9
Informed Consent	X								
Inclusion & Exclusion Criteria	X								
Demographics	X								
Vital Signs	X								
Physical Exam	X		X			X	X	X	X
Medical History	X			X	X	X	X	X	X
Hospitalization/Cardiovascular History	X								
AF History	X								
ECG	X		X			X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X
CHA2DS2-VASc and CHADS2 Score	X								
NYHA Scale	X								
QOL Assessment	X					X	X	X	
Pregnancy Test	X								
LA Size and LVEF Imaging	X								
LA Thrombus Imaging		X							
Ablation Assessments		X							
Device Deficiency		X							
TTE		X							
Concomitant Medications	X	X	X	X	X	X	X	X	X
Repeat Ablation					X	X	X	X	X

	Pre-Procedure	Ablation / Discharge		Phone / Virtual	Follow-Up Visits				
	Screening/Baseline	Study Ablation (Day 0)	Discharge	7 Days (Day 7-10)	1 Month (Day 23-37)	3 Month (Day 76-104)	6 Month (Day 150-210)	12 Month (Day 335-395)	Unscheduled
AF/AT/AFL Recurrence			X	X	X	X	X	X	X
TTM					X	X	X	X	
24 Hour Holter							X	X	
Completion/Discontinuation Form		X	X	X	X	X	X	X	

### 3. Clinical Endpoints

The endpoints for the study were as follows:

#### ***Primary Safety Endpoints***

The primary safety endpoint was the incidence of primary adverse events (PAEs) occurring within 7 days of an ablation procedure which used the VARIPULSE Catheter and TRUPULSE Generator per protocol.

Primary adverse events included the following adverse events:

- Death (device or procedure related)
- Atrio-Esophageal Fistula\*
- Cardiac Tamponade\*\* / Perforation\*\*
- Myocardial Infarction
- Stroke / Cerebrovascular Accident
- Thromboembolism
- Transient Ischemic Attack
- Phrenic Nerve Injury / Diaphragmatic Paralysis
- Heart Block
- PV Stenosis<sup>+</sup>
- Pulmonary Edema (Respiratory Insufficiency)
- Vagal Nerve Injury / Gastroparesis

- Pericarditis
- Major Vascular Access Complication / Bleeding

\* *Atrio-esophageal fistula that occurred greater than one week (7 days) post-procedure and up to 90 days post-procedure was considered and analyzed as a PAE.*

\*\* *Cardiac Tamponade/Perforation occurring within 30 days of the AF ablation process was considered a PAE*

+ *Pulmonary Vein Stenosis was considered as a PAE if it occurred anytime during the 12- month follow up period*

### *Hypothesis*

The primary safety endpoint will be assessed by testing the hypotheses:

$H_0: p_S \geq 0.12$  vs.  $H_A: p_S < 0.12$ , where  $p_S$  is the proportion of patients with PAE. The primary safety endpoint will be evaluated using the exact two-sided 95% confidence interval for the PAE rate. If the upper bound of the exact confidence interval of the primary safety rate is less than the performance goal of 12%, the study would have been considered to have demonstrated safety in the PAF population.

### *Analysis Methods*

In the Pivotal main phase (excluding roll-in), hypothesis testing was performed in the modified intent-to-treat (mITT, all subjects enrolled in the Pivotal main phase who meet eligibility criteria and have the study catheter inserted) analysis set. Subjects with non-missing PAE outcome data were included in the primary analysis. The primary safety endpoint was evaluated using the exact test for a binomial proportion at a one-sided significance level of 2.5%. If the upper bound of the exact two-sided 95% confidence interval of the primary safety endpoint rate is less than the performance goal of 12%, the study would be considered to have demonstrated safety.

### ***Primary Effectiveness Endpoints***

The primary effectiveness endpoint was freedom from electrocardiographically documented atrial fibrillation, atrial tachycardia, or atrial flutter (AF/AT/AFL) episodes during the effectiveness evaluation period (Day 91-365), and freedom from the following failure modes:

- Acute procedural
  - Failure to confirm entrance block in all pulmonary veins at the end of the procedure.
- Repeat ablation
  - More than 1 repeat ablation procedure for AF/AT/AFL during the 3-Month Blanking Period (Day 0-90 post index procedure).

- Any repeat ablation procedure for AF/AT/AFL during the evaluation period.
- Non-study Catheter
  - Use of a non-study catheter (NSC) to treat pulmonary vein targets to achieve isolation of clinically relevant PVs and/or to ablate left atrial non-PV AF targets during the index procedure.
  - Use of a non-study catheter to treat pulmonary vein targets to achieve isolation of clinically relevant PVs during repeat procedure in the blanking period.
- Anti-arrhythmic Drug
  - Taking a new AAD (Class I & III) for AF/AT/AFL or taking a previously failed Class I/III AAD at a greater than the highest ineffective historical dose for AF/AT/AFL beyond the 3-month follow-up visit window.
- Continuous AF/AT/AFL
  - Continuous AF/AT/AFL on a standard 12-lead ECG during the effectiveness evaluation period.
- DC Cardioversion
  - Any DC cardioversion procedure during the evaluation period for documented for AF/AT/AFL recurrences.

### *Hypothesis*

The primary effectiveness endpoint will be assessed by testing the hypotheses:  $H_0: p_E \leq 0.50$  vs.  $H_A: p_E > 0.50$ , where  $p_E$  is the proportion of subjects that are free from primary effectiveness failures at 12-month follow-up. The primary effectiveness endpoints will be evaluated using the exact two-sided 95% confidence interval for the effectiveness success rate. If the lower bound of the exact confidence interval of the primary effectiveness success rate was greater than the performance goal of 50%, the study would have been considered to have demonstrated effectiveness.

## *Analysis*

In the Pivotal main phase, hypothesis testing was performed in the Per Protocol (PP, subjects enrolled and did not have any protocol deviations that would affect integrity of the data) analysis set. Subjects with non-missing primary effectiveness endpoint (PEE) outcome data will be included in the primary analysis. The primary effectiveness endpoint will be evaluated using the exact test for a binomial proportion at one-sided significance level of 2.5%. If the lower bound of the exact two-sided 95% confidence interval of the primary effectiveness success rate is greater than the performance goal of 50%, the study will be considered to have demonstrated effectiveness.

### ***Secondary Effectiveness Endpoints***

- QOL (AFEQT) Improvement:
  - Improvement in total score of Atrial Fibrillation Effect on Quality-of-Life Questionnaire (AFEQT) at 12M post procedure compared to baseline score.

### ***Additional Safety Endpoints***

- Incidence of Unanticipated Adverse Device Effects (UADEs).
- Incidence of Serious Adverse Events (SAEs) within 7 days (early onset), >7 to 30 days (peri-procedural) and >30 days (late onset) of initial ablation.
- Incidence of bleeding complication (ISTH definitions): a) major, b) clinically relevant non-major and c) minor bleeding.

### ***Additional Effectiveness Endpoints***

- Acute Procedural Success defined as the percent of subjects with electrical isolation of all PVs with confirmed entrance block at the end of the procedure.
- Freedom from Documented Atrial Tachyarrhythmia off Class I/III AAD defined as freedom from electrocardiographically documented atrial tachyarrhythmia episodes during the effectiveness evaluation period and off Class I/III AAD beyond the 3-month follow-up visit window.
- 12 Months Single Procedure Treatment Success defined as freedom from electrocardiographically documented symptomatic AF/AFL/AT recurrence during the effectiveness evaluation period following a single index ablation procedure and freedom from all other failure modes, including acute

procedural failure, non-study catheter failure, AAD failure, and DCCV failure defined in the primary effectiveness endpoint. Any repeat ablation procedure for AF/AT/AFL during follow-up would result in 12 Months single procedure treatment failure.

- Clinical Success defined as the freedom from documented symptomatic atrial tachyarrhythmia episodes based on electrocardiographic data ( $\geq 30$  seconds on ECG or sponsor provided cardiac event monitor (CEM) or Holter device (HM)) during the effectiveness evaluation period (Day 91-Day 365).

**B. Accountability of PMA Cohort**

At the time of database lock, of 291 patients enrolled in the PMA study, 277 had the study catheter inserted, and 269 patients were available for analysis at the completion of the study, the 12-month post-operative visit. The disposition definitions for subjects are presented in Table 4, and information on subject disposition is presented in Table 5.

**Table 4: Subject Disposition**

<b>Disposition</b>	<b>Definition</b>
Enrolled Subjects	Subjects who signed the informed consent
Excluded Subjects	Subjects who were enrolled but never underwent insertion of the study catheter
Evaluable Subjects	All enrolled subjects who have the study catheter inserted.
Discontinued Subjects	Evaluable subjects who have the study catheter inserted but do not undergo ablation (i.e., no PFA energy is delivered with the study catheter). Discontinued subjects will remain in follow-up for 3 months post catheter insertion.
Lost to Follow-up Subjects	Subjects who were evaluable, but contact was lost after the most recent follow-up visits (despite 3 documented attempts to contact the subject)
Withdrawn / Early Termination Subjects	Subjects who withdrew consent for study participation or were withdrawn by the investigator or were terminated from the study prior to completion of all follow-up visits
Completed Subjects	Enrolled subjects who have not been excluded, discontinued, lost-to-follow-up or withdrawn/ early terminated prior to the final study visit and have completed the 12-month follow up visit.

**Table 5: Subject Accountability**

Subject Enrollment	Pilot	Roll-in	Main study
Enrolled Subjects	22	71	291
Excluded Subjects	1	7	14
Study Catheter Inserted	21	64	277
Discontinued Subjects	0	0	1
Death	0	1	0
Withdrawn	1	1	2
Early Termination Subjects	0	0	0
Lost to Follow Up Subjects	0	0	5
Completed Subjects	20	62	269

**C. Study Population Demographics and Baseline Parameters**

The demographics of the study population (depicted in Table 6 and Table 7) are typical for a pivotal, single-arm, catheter ablation study performed in the US.

**Table 6: Subject Demographics**

Variable	Statistics		
	Pivotal Main Phase Safety Analysis Set, N=277	Pivotal Main Phase mITT Analysis Set, N=274	Pivotal Main Phase, Per-Protocol Analysis Set, N=255
<b>Age (years)</b>			
n	277	274	255
Mean ± Standard Deviation	61.5 ± 10.30	61.5 ± 10.27	61.6 ± 10.28
Median	64.0	64.0	64.0
Q1 / Q3	57.0 / 68.0	57.0 / 68.0	57.0 / 68.0
Min / Max	19 / 76	19 / 75	19 / 75
<b>Sex, n/N (%)</b>			
Male	178 / 277 (64.3%)	176 / 274 (64.2%)	163 / 255 (63.9%)
Female	99 / 277 (35.7%)	98 / 274 (35.8%)	92 / 255 (36.1%)
Of child-bearing potential	8 / 99 (8.1%)	8 / 98 (8.2%)	7 / 92 (7.6%)
Permanently sterilized [or infertile]	6 / 99 (6.1%)	6 / 98 (6.1%)	6 / 92 (6.5%)
Postmenopausal	85 / 99 (85.9%)	84 / 98 (85.7%)	79 / 92 (85.9%)

Variable	Statistics		
	Pivotal Main Phase Safety Analysis Set, N=277	Pivotal Main Phase mITT Analysis Set, N=274	Pivotal Main Phase, Per-Protocol Analysis Set, N=255
<b>Ethnicity, n/N (%)</b>			
Hispanic or Latino	7 / 277 (2.5%)	7 / 274 (2.6%)	6 / 255 (2.4%)
Not Hispanic or Latino	215 / 277 (77.6%)	213 / 274 (77.7%)	196 / 255 (76.9%)
Not Reported	55 / 277 (19.9%)	54 / 274 (19.7%)	53 / 255 (20.8%)
<b>Race, n/N (%)</b>			
American Indian/Alaska Native	4 / 277 (1.4%)	4 / 274 (1.5%)	3 / 255 (1.2%)
Asian	12 / 277 (4.3%)	12 / 274 (4.4%)	11 / 255 (4.3%)
Black or African American	7 / 277 (2.5%)	7 / 274 (2.6%)	6 / 255 (2.4%)
White	228 / 277 (82.3%)	226 / 274 (82.5%)	211 / 255 (82.7%)
Race not reported	25 / 277 (9.0%)	24 / 274 (8.8%)	23 / 255 (9.0%)
<b>BMI (kg/m<sup>2</sup>)</b>			
n	277	274	255
Mean	28.74 ± 5.912	28.69 ± 5.850	28.75 ± 5.924
Median	27.90	27.95	28.00
Q1 / Q3	24.80 / 31.90	24.80 / 31.90	24.80 / 32.00
Min / Max	17.6 / 56.6	17.6 / 56.6	17.6 / 56.6

**Table 7: Baseline Characteristics**

Variable	Statistics		
	Pivotal Main Phase Safety Analysis Set, N=277	Pivotal Main Phase mITT Analysis Set, N=274	Pivotal Main Phase, Per-Protocol Analysis Set, N=255
<b>Cardiovascular Medical History</b>	209 / 277 (75.5%)	207 / 274 (75.5%)	193 / 255 (75.7%)
Congestive heart failure	9 / 277 (3.2%)	8 / 274 (2.9%)	8 / 255 (3.1%)
Coronary disease	55 / 277 (19.9%)	54 / 274 (19.7%)	49 / 255 (19.2%)
Vascular disease	17 / 277 (6.1%)	17 / 274 (6.2%)	17 / 255 (6.7%)
Myocardial infarction	8 / 277 (2.9%)	8 / 274 (2.9%)	7 / 255 (2.7%)
Hypertension (systemic)	148 / 277 (53.4%)	147 / 274 (53.6%)	136 / 255 (53.3%)
Pulmonary hypertension	6 / 277 (2.2%)	6 / 274 (2.2%)	6 / 255 (2.4%)
Cardiomyopathy	8 / 277 (2.9%)	8 / 274 (2.9%)	8 / 255 (3.1%)
Left ventricular hypertrophy	4 / 277 (1.4%)	4 / 274 (1.5%)	4 / 255 (1.6%)

Variable	Statistics		
	Pivotal Main Phase Safety Analysis Set, N=277	Pivotal Main Phase mITT Analysis Set, N=274	Pivotal Main Phase, Per-Protocol Analysis Set, N=255
Significant valvular disease	1 / 277 (0.4%)	1 / 274 (0.4%)	1 / 255 (0.4%)
Hyperlipidemia	135 / 277 (48.7%)	133 / 274 (48.5%)	124 / 255 (48.6%)
<b>Documented Thromboembolic Events</b>	10 / 277 (3.6%)	9 / 274 (3.3%)	8 / 255 (3.1%)
Transient ischemic attack (TIA)	8 / 277 (2.9%)	7 / 274 (2.6%)	6 / 255 (2.4%)
Stroke	1 / 277 (0.4%)	1 / 274 (0.4%)	1 / 255 (0.4%)
<b>Other Medical History [+]</b>	93 / 277 (33.6%)	92 / 274 (33.6%)	86 / 255 (33.7%)
Type II Diabetes	30 / 277 (10.8%)	30 / 274 (10.9%)	29 / 255 (11.4%)
Obstructive sleep apnea (OSA)	77 / 277 (27.8%)	76 / 274 (27.7%)	71 / 255 (27.8%)
OSA treated	58 / 277 (20.9%)	57 / 274 (20.8%)	53 / 255 (20.8%)
CPAP for OSA	48 / 277 (17.3%)	48 / 274 (17.5%)	44 / 255 (17.3%)
<b>CHA<sub>2</sub>DS<sub>2</sub>-VASc Score</b>	1.7 ± 1.29	1.7 ± 1.26	1.7 ± 1.26
<b>AAD Failed - Class I &amp; III Mean ± SD</b>	1.0 ± 0.22	1.1 ± 0.22	1.0 ± 0.22
<b>Duration of symptomatic paroxysmal AF (months) Mean ± SD</b>	52.69 ± 73.39	52.31 ± 72.828	52.14 ± 73.140
<b>Symptomatic PAF episodes within 12 months</b>	42.9 ± 90.15	43.4 ± 90.54	42.0 ± 90.43
<b>Arrhythmia other than paroxysmal AF, n/N (%)</b>			
Atrial Tachycardia Origin Undefined	8 / 277 (2.9%)	8 / 274 (2.9%)	8 / 255 (3.1%)
Atrial Flutter Typical Right	16 / 277 (5.8%)	16 / 274 (5.8%)	15 / 255 (5.9%)
Atrial Flutter Origin Undefined	29 / 277 (10.5%)	29 / 274 (10.6%)	24 / 255 (9.4%)
AV Node Re-Entry Tachycardia	1 / 277 (0.4%)	1 / 274 (0.4%)	1 / 255 (0.4%)
<b>LA Diameter (mm)</b>	38.08 ± 5.797	38.06 ± 5.807	38.04 ± 5.847
<b>LVEF (%)</b>	60.7 ± 5.95	60.7 ± 5.90	60.5 ± 5.87

## **D. Safety and Effectiveness Results**

### **1. Safety Results**

The analysis of safety was based on the modified intent-to-treat cohort of 274 patients available through 3 months post-procedure. The key safety outcomes and adverse effects for this study are presented below.

#### **Adverse effects that occurred in the PMA clinical study:**

The primary safety endpoint for this study was defined as the incidence of early onset (within 7 days of ablation procedure) Primary AEs for subjects undergoing a study ablation procedure. Per study protocol, the primary safety analysis was based on the primary safety event rate in the Pivotal Phase Main mITT analysis set (N=274) as the primary analysis population.

**Error! Reference source not found.** displays a summary for the primary safety endpoint in subjects with non-missing outcomes in the mITT analysis set. The PAE rate was 2.9% and the exact one-sided 97.5% upper confidence bound was 5.7%, which is less than the pre-specified performance goal of 12%. Therefore, the results indicate that the study met the pre-defined performance goal for the primary safety endpoint.

The primary safety analysis was repeated in the Pivotal Main Safety analysis set (i.e., all pivotal main phase subjects with the study catheter inserted) as a sensitivity analysis. Similar to the mITT analysis set, a total of eight subjects experienced nine PAEs in the Safety analysis set. There were no additional PAEs observed compared to the mITT analysis set. For Pivotal Main Phase subjects in the Safety analysis set, the PAE rate remained at 2.9% and the exact one-sided 97.5% upper confidence bound was 5.7%, which maintains below the pre-specified performance goal of 12%.

The PAEs reported in this study were cardiac tamponade/perforation (n = 3), major vascular access complication/bleeding (n = 2), pericarditis (n = 1), stroke/cerebrovascular accident (n = 2) and transient ischemic attack (n = 1).

There were NO incidents of device or procedure-related death, atrio-esophageal fistula, myocardial infarction, thromboembolism, phrenic nerve injury/diaphragmatic paralysis, heart block, pulmonary vein stenosis, pulmonary edema, or vagal nerve injury/gastroparesis.

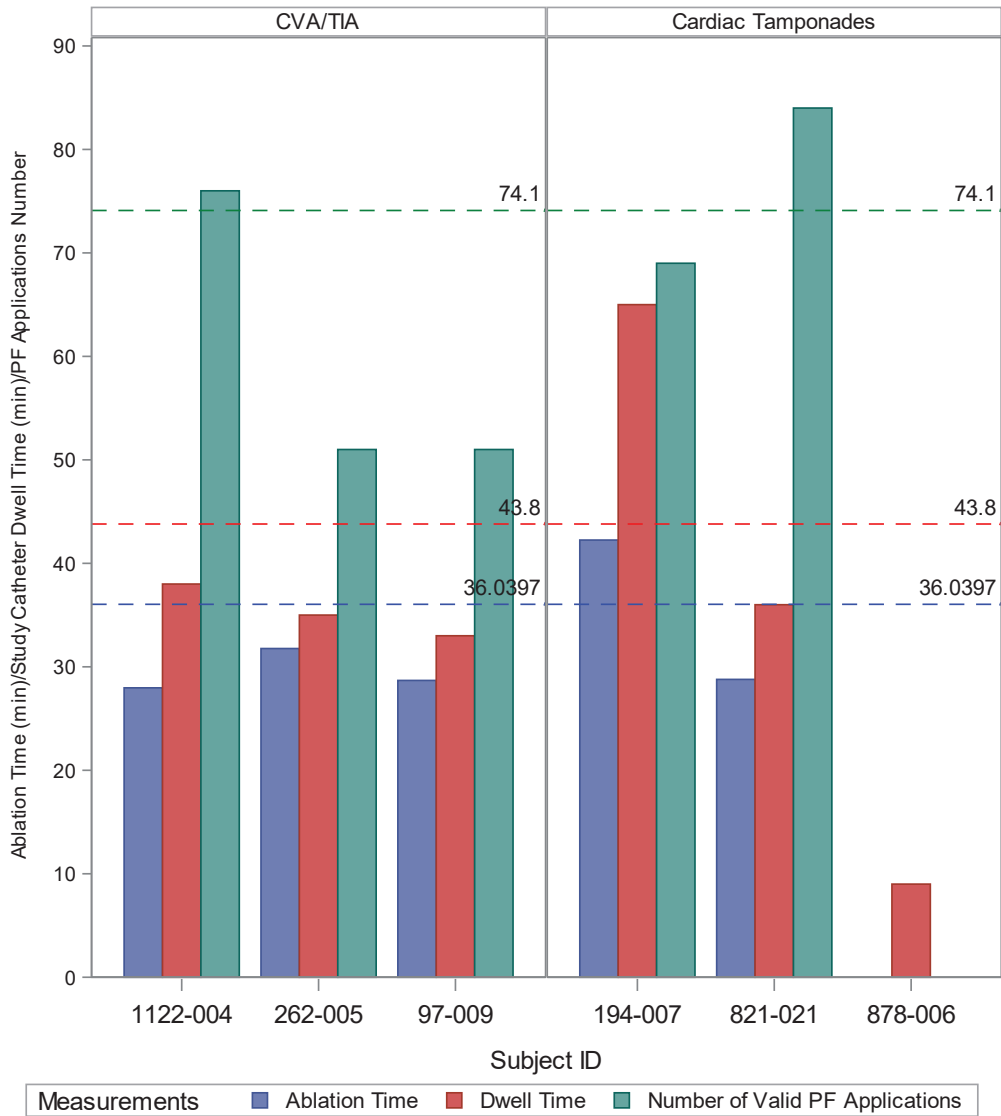
**Table 8: Primary Safety Endpoint (Pivotal Main Phase mITT Analysis Set, N=274)**

Variable	Number of Subjects with Events	Number of Events	Event Rate n/N (%) [1]	Exact One-Sided 97.5% Upper Confidence Bound
<b>Primary Adverse Event</b>	8	9	8 /272 (2.9%)	5.7%
<b>Type of Primary Adverse Event</b>				
Cardiac Tamponade/Perforation	3*	3	3 /272 (1.1%)	
Major Vascular Access Complication/Bleeding	2	2	2 /272 (0.7%)	
Pericarditis	1*	1	1 /272 (0.4%)	
Stroke/Cerebrovascular Accident	2	2	2 /272 (0.7%)	
Transient Ischemic Attack	1	1	1 /272 (0.4%)	

[1] Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

\*One (1) subject experienced two (2) PAEs: Cardiac tamponade/perforation and Pericarditis.

Figure 2 presents the ablation time, study catheter dwell time, and number of applications for subjects experiencing a cardiac tamponade or CVA (stroke) or TIA as PAE compared to the mean values for subjects in the Pivotal Phase Main Safety analysis set. The procedural workflow in subjects who experienced a PAE appeared to be comparable to that in other subjects in the Pivotal Main Phase Safety analysis set who did not experience any PAE.



**Figure 2: Comparison of Ablation Time (min), Study Catheter Dwell Time (min), and Number of PF Applications in subject with Cardiac Tamponades and CVA/TIA.**

***Serious Non-Primary AEs***

Table 9 summarizes the SAEs (by causality and body system) occurring within 30 days of a study ablation procedure that were not classified as Primary AEs by protocol definition.

**Table 9: Serious Non-Primary AEs (Occurring 0-30 Days Post Index/Repeat Ablation Procedure) by Severity, Causality and Outcome (Pivotal Main Phase Safety Analysis Set, N=277)**

Severity	Relationship to VARIPULSE™ Catheter	Relationship to TRUPULSE™ Generator	Relationship to Procedure	Outcome	AE Term
<b>0-7 days Post Ablation Procedure</b>					
Severe	Causal Relationship to Device	Causal Relationship to Device	Causal Relationship to Procedure	Recovered/Resolved	Cardiac arrest
Moderate	Not Device Related	Not Device Related	Causal Relationship to Procedure	Recovered/Resolved	Urinary retention
	Not Device Related	Not Device Related	Possible Procedure Related	Recovered/Resolved	Migraine
	Not Device Related	Not Device Related	Not Procedure Related	Recovered/Resolved	Atrial fibrillation
	Not Device Related	Not Device Related	Not Procedure Related	Recovered/Resolved	Diverticulitis
	Not Device Related	Not Device Related	Not Procedure Related	Recovered/Resolved	Pericardial effusion
	Not Device Related	Not Device Related	Not Procedure Related	Recovered/Resolved	Urinary retention
	Not Device Related	Not Device Related	Not Procedure Related	Recovered/Resolved	Wound secretion
	Not Device Related	Not Device Related	Not Procedure Related	Recovered/Resolved with sequelae	Pneumonia
Mild	Not Device Related	Not Device Related	Not Procedure Related	Recovered/Resolved	Lower gastrointestinal hemorrhage
<b>8-30 days Post Ablation Procedure</b>					
Mild	Possible Device Related	Possible Device Related	Probable Procedure Related	Recovered/Resolved	Pleural effusion

***Subject Deaths***

One roll-in subject died of out-of-hospital cardiac arrest with a suspected diagnosis of acute myocardial infarction on day 39 post study procedure without immediate complications or significant findings on 7-day and 1-month follow-up

evaluation. No autopsy was performed. The death was classified as not related to either the study device(s) or procedure by the investigator. .

**Primary Safety by Sex**

Table 10 summarizes the primary safety endpoint by sex for subjects in the Pivotal Main Phase mITT analysis set. The difference in PAE rates between male and female subjects was significant at the 0.15 alpha level (p-value=0.027 < 0.15).

**Table 10: Primary Safety Endpoint by Sex  
(Pivotal Main Phase mITT Analysis Primary Set, N=274)**

Primary Safety Endpoint	Male	Female	P-value <sup>[1]</sup>
n/N	2 / 174	6 / 98	0.027
% <sup>[1]</sup>	1.1%	6.1%	
95% Confidence Interval	(0.1%, 4.1%)	(2.3%, 12.9%)	

[1] By Fisher's exact test.

Further analysis of the device related PAEs by sex. Table 11 summarizes the primary safety endpoint related to the study devices (VARIPULSE Catheter and/or TRUPULSE Generator) by sex for subjects in the Pivotal Main Phase mITT analysis set. The difference between sex narrowed. The device related PAE rates were 1.1% in male subjects and 4.1% in female subjects.

**Table 11: Primary Safety Endpoint Related to Study Device(s) by Sex  
(Pivotal Main Phase mITT Analysis Set, N=274)**

Primary Safety Endpoint	Male	Female
n/N	2 / 174	4 / 98
%	1.1%	4.1%

2. Effectiveness Results

The analysis of effectiveness was based on the 255 (Per Protocol) evaluable patients at the 12-month time point. Procedural data are depicted in Table 12, Table 13, and Table 14.

*Procedural Data*

**Table 12: Summary of PFA Applications, Ablation Duration, and PFA Application Time**

Variable	Statistics (Mean ± SD)		
	Pivotal Main Phase Safety Analysis Set, N=277	Pivotal Main Phase mITT Analysis Set, N=274	Pivotal Main Phase, Per-Protocol Analysis Set, N=255
Total LA mapping time (min)	7.67 ± 5.031	7.67 ± 5.057	7.83 ± 5.044
Total Left Atrium study catheter dwell time (min)	43.83 ± 18.193	44.02 ± 18.192	43.27 ± 17.765
Total procedure time (min)	95.14 ± 37.189	95.23 ± 37.334	94.98 ± 37.448
Total duration of fluoroscopy at end of procedure (min)	9.99 ± 12.199	10.06 ± 12.237	9.63 ± 12.375
Fluid delivered via study catheter (mL)	254.89 ± 131.980	255.53 ± 132.295	252.90 ± 132.858

**Table 13: Summary of Ablation Procedure Parameters**

Variable	Statistics (Mean ± SD)		
	Pivotal Main Phase Treated Subjects Set, N=277	Pivotal Main Phase mITT Analysis Set, N=274	Pivotal Main Phase, Per-Protocol Analysis Set, N=255
<b>Number of Valid PFA Applications</b>	74.1 ± 19.29	74.2 ± 19.36	71.7 ± 15.57
<b>Total Ablation Duration (min)*</b>	36.04 ± 19.730	36.18 ± 19.788	35.14 ± 19.443
<b>Total Valid PFA Application Time (sec)**</b>	17.96 ± 4.674	17.98 ± 4.689	17.36 3.771

**Table 14: Ablation Sites Targeted**

Ablation Sites Targeted	Statistics (n/N) (%)		
	Pivotal Main Phase Treated Subjects Set, N=276	Pivotal Main Phase mITT Analysis Set, N=274	Pivotal Main Phase, Per-Protocol Analysis Set, N=255
<b>Total</b>	276 / 276 (100.0%)	273 / 274 (99.6%)	255 / 255 (100.0%)
<b>PVs Only</b>	213 / 276 (77.2%)	210 / 274 (76.6%)	200 / 255 (78.4%)
<b>PVs + Non-PV with VARIPULSE Catheter</b>	18 / 276 (6.5%)	18 / 274 (6.6%)	17 / 255 (6.7%)
Posterior Wall, Segmental	16 / 276 (5.8%)	16 / 273 (5.9%)	15 / 255 (5.9%)
Other AF Foci	1 / 276 (0.4%)	1 / 273 (0.4%)	1 / 255 (0.4%)
Other Linear Lesion	1 / 276 (0.4%)	2 / 273 (0.7%)	2 / 255 (0.8%)

### *Arrhythmia Monitoring Compliance*

Composite arrhythmia monitoring compliance was calculated per the protocol required assessment schedule of TTM/CEM, ECG and HM. Composite arrhythmia monitoring compliance was 99.2% at 6-Month and 96.8% at 12-Month post-procedure.

### *Primary Effectiveness Endpoint*

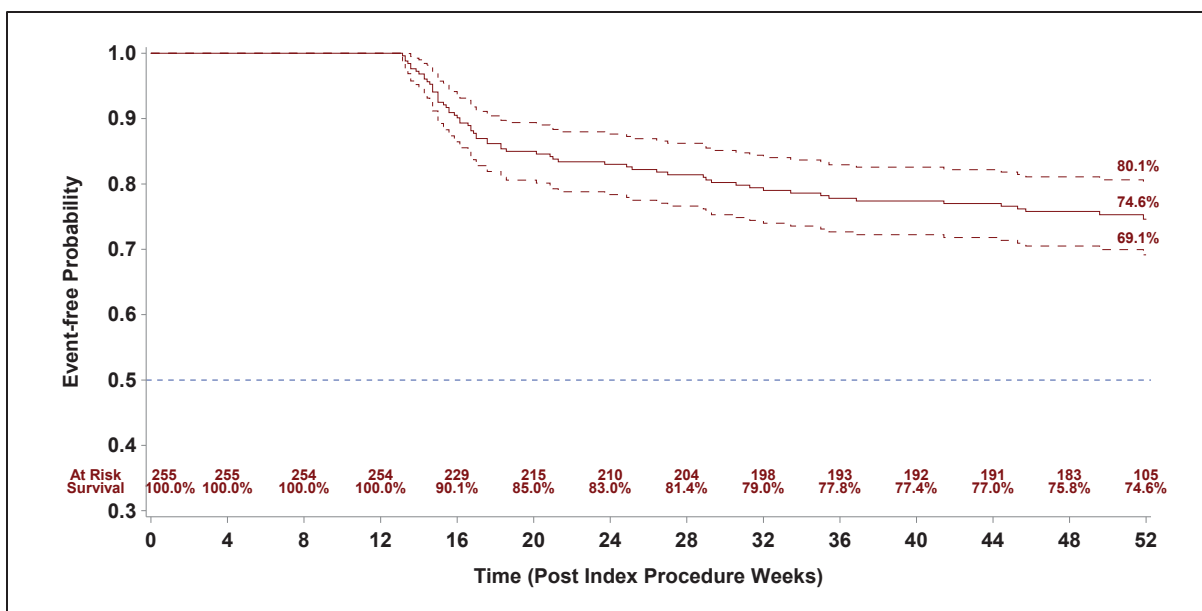
#### *Primary Analysis*

Per study protocol, the primary effectiveness analysis was based on primary effectiveness success using the Per Protocol Analysis set as the primary analysis population. As shown in Table 15, the primary effectiveness outcome for the Pivotal Main Phase Per Protocol Analysis. The success rate was 74.4% and the exact one-sided 97.5% lower confidence bound was 68.5%, which is greater than the pre-specified performance goal of 50%. Therefore, the results indicate that the study met the primary effectiveness endpoint.

**Table 15: Primary Effectiveness Endpoint  
(Pivotal Main Phase Per Protocol Analysis Set, N=255)**

<b>Outcome</b>	<b>Number of Subjects</b>	<b>Success Rate n/N (%)</b>	<b>Exact One-Sided 97.5% Lower Confidence Bound</b>
<b>Success</b>	183	183/246 (74.4%)	68.5%
<b>Failure</b>	63		
<b>Missing</b>	9		

Kaplan-Meier freedom from effectiveness failure for subjects (Figure 3) in the Pivotal Main Phase Per Protocol Analysis set indicated a success rate of 74.6% at 12 months.



**Figure 3: Kaplan-Meier Analysis of Time to Primary Effectiveness Failure [1]  
(Pivotal Main Phase, Phase Per Protocol Analysis Set, N=255)**

Table 16 summarizes the first failure reason for subjects in the Pivotal Main Phase Per Protocol analysis set. For first failures, if a subject had more than one failure event, only the earliest failure event was summarized. For total failures, if a subject had failed for multiple modes, the subject was counted in all applicable failure modes.

The first failure events reported among 63 primary effectiveness failures included documented recurrence of atrial tachyarrhythmias (60/63) and new AAD failure (3/63). Among the 89 total failure events reported, 61 were documented recurrence of atrial tachyarrhythmias, 19 repeat ablation, and 8 AAD failures.

**Table 16: Primary Effectiveness Failures  
(Pivotal Main Phase Per Protocol Analysis Set, N=255)**

<b>Outcome</b>	<b>Number of Subjects</b>
<b>First Failures<sup>[1]</sup></b>	63
Acute Procedural Failure <sup>[2]</sup>	0
Recurrence <sup>[3]</sup>	60
Atrial Fibrillation	47
Atrial Flutter	11
Atrial Tachycardia	2
Repeat Ablation Failure <sup>[4]</sup>	0
NSC Failure <sup>[5]</sup>	0
AAD Failure <sup>[6]</sup>	3
AAD Failure - New Drug	3
DCCV Failure <sup>[7]</sup>	0

[1] First failures: if a subject has at least 1 failure event, only the earliest failure event is considered and summarized by its failure mode. Total Failures: if a subject has failed for multiple modes, the subject will be counted in all applicable failure modes.

[2] Acute procedural failure is defined as failure to confirm entrance block in all PVs except those that are silent and/or cannot be cannulated post-procedure, or failure to have PFA delivery with the study catheter due to IRE system malfunctions.

[3] Recurrence is defined as documented (symptomatic and asymptomatic) atrial tachyarrhythmia (AF, AT or AFL of unknown origin) episodes based on electrocardiographic data (>=30 seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period.

[4] Repeat ablation failure is defined as more than 1 repeat ablation procedure for AF/AT/ AFL of unknown origin during the blanking period, or any repeat ablation procedure for AF/AT/ AFL of unknown origin during the evaluation period.

[5] NSC failure is defined as use of a NSC to treat PV targets to achieve isolation of clinically relevant PVs (all PVs except those that are silent and/or cannot be cannulated) and/or ablation of left atrial non-PV AF targets during the index procedure, or use of a NSC to treat PV targets to achieve isolation of clinically relevant PVs (all PVs except those that are silent and/or cannot be cannulated) during a repeat procedure in the blanking period.

[6] AAD failure is defined as taking a new AAD (Class I and III) for atrial tachyarrhythmia (AF, AT or AFL of unknown origin), or a previously failed AAD at a greater than the highest ineffective historical dose for AF/AFL/AT during the effectiveness evaluation period.

[7] DCCV failure is defined as Any DCCV procedure during the effectiveness evaluation period for documented atrial tachyarrhythmia recurrences ascertained through protocol specified arrhythmia monitoring methods (12 lead ECG, CEM and Holter).

### *Sensitivity Analysis*

The analysis of primary effectiveness endpoint was repeated in all Pivotal Main Phase mITT and All Treated analysis sets as a sensitivity analysis. The success rate was 72.7% and the exact one-sided 97.5% lower confidence bound was 66.9%, which is also greater than the pre-specified performance goal of 50% (Table 17). The results suggested that the success rates in all three analysis cohorts met the effectiveness performance goal.

**Table 17: Primary Effectiveness Endpoint**

Pivotal Main Phase	Outcome	Number of Subjects	Success Rate n/N (%) <sup>[1]</sup>	Exact One-Sided 97.5% Lower Confidence Bound
mITT (N=274)	Success	192	192/264 (72.7%)	66.9%
	Failure	72		
	Missing <sup>[2]</sup>	10		
All Treated (N=276)	Success	194	194/267 (72.7%)	66.9%
	Failure	73		
	Missing <sup>[2]</sup>	9		

[1] N represents the number of subjects who either 1) experienced a primary effectiveness failure, 2) completed 12-months of follow-up, or 3) had ECG, CEM, or HM data beyond 335 days after the index procedure.

[2] Subjects who did not experience a primary effectiveness failure and did not complete 12-months of follow-up or have ECG, CEM, or HM data beyond 335 days of the index procedure.

***Secondary Effectiveness Endpoint***

Table 18 presents the change in overall AFEQT scores at 12-months compared to baseline. There was a significant improvement in AFEQT score at 12-months compared to baseline for subjects in the Per Protocol Analysis set (p<0.001) and the mITT Analysis set (p<0.001).

**Table 18: Change in Overall AFEQT Score at 12 Months**

AFEQT Questionnaire	Pivotal Main Phase Per Protocol Analysis Set (N=255)		Pivotal Main Phase mITT Analysis Set (N=274)
	Statistics	P-value <sup>[1]</sup>	Statistics
Change from Baseline			
Mean	32.033	<.0001	32.077
95% Confidence Interval	(29.092, 34.973)		(29.247, 34.906)

[1] By paired t-test

***Additional Effectiveness Endpoint***

***Acute Procedural Success***

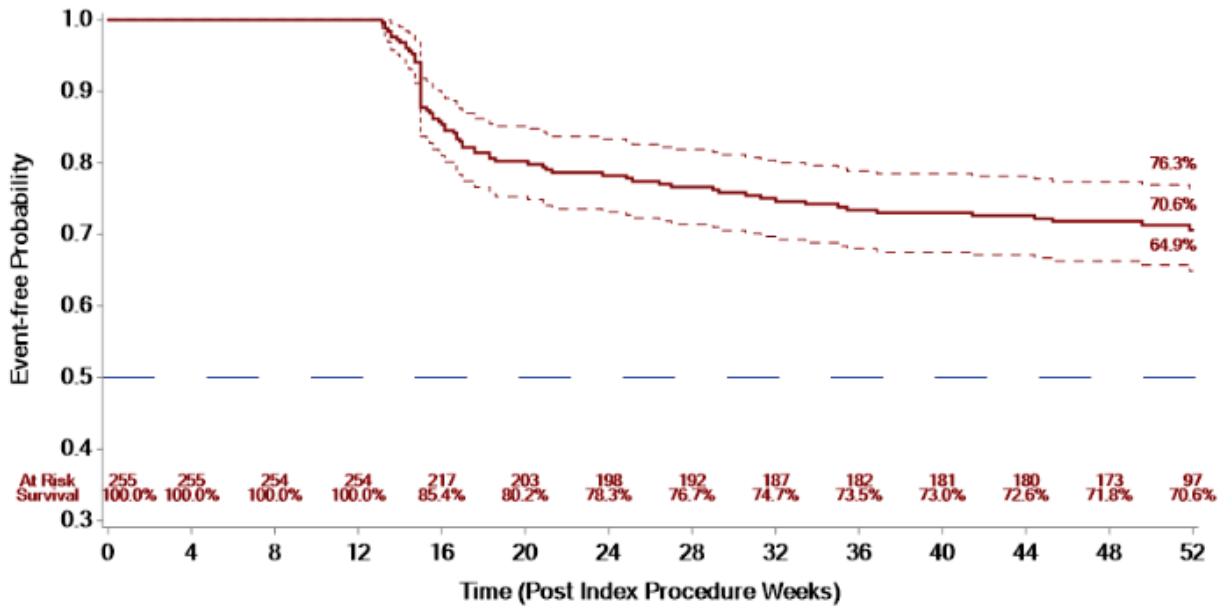
Table 19 presents the acute procedural success (confirmation of entrance block in all PVs) among subjects treated with the study catheter in the Per Protocol and mITT Analysis sets. Acute procedural success was defined as confirmation of entrance block in all PVs. One (1) subject in the mITT analysis set who was discontinued due to non-PFA system related reasons prior to PFA delivery was treated as missing. All subjects that were treated (i.e., energy delivered) with the study catheter achieved acute procedural success

**Table 19: Acute Procedural Success**

Pivotal Main Phase	Number of Subjects	Number of Successful Subjects	Success Rate n/N (%)
Per Protocol Analysis Set (N=255)	255	255	255/255 (100.0%)
MITT Analysis Set (N=274)	273	273	273/273 (100.0%)

*Freedom from documented atrial tachyarrhythmia off Class I/III AAD*

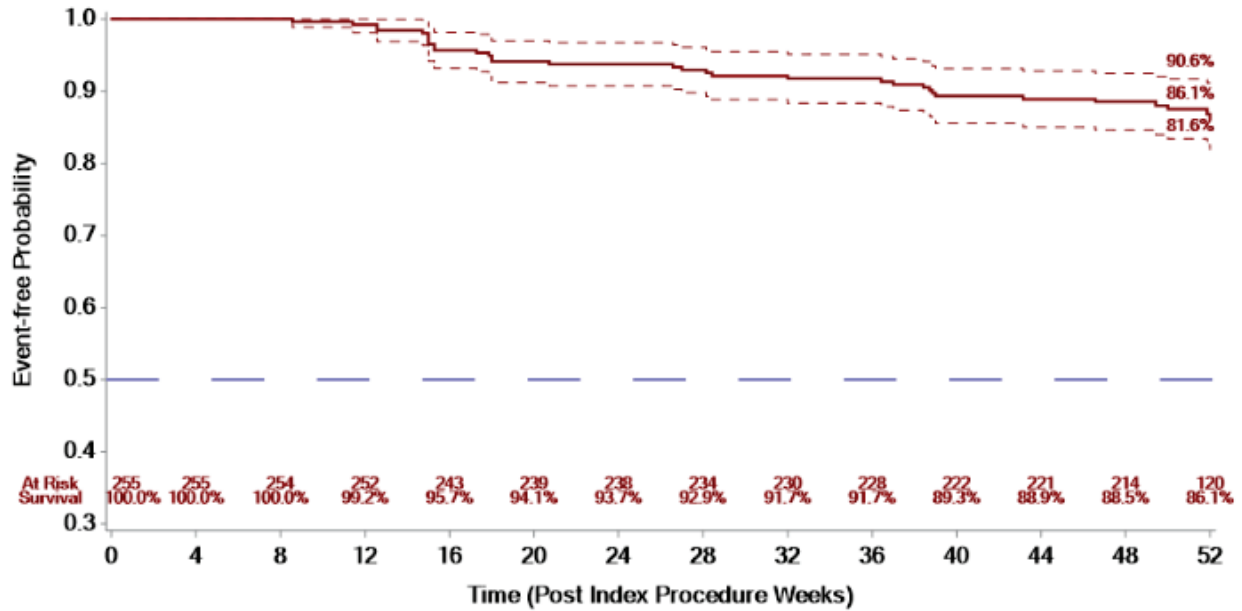
Kaplan-Meier estimates (Figure 4) used to characterize the time to first documented (symptomatic and asymptomatic) atrial tachyarrhythmia episodes off Class I/III AAD was 70.6% in the Pivotal Main Phase Per Protocol analysis set.



**Figure 4: Kaplan-Meier Analysis of time to Documented Recurrence and Off AAD (Pivotal Main Phase Per Protocol Analysis Set, N = 255)**

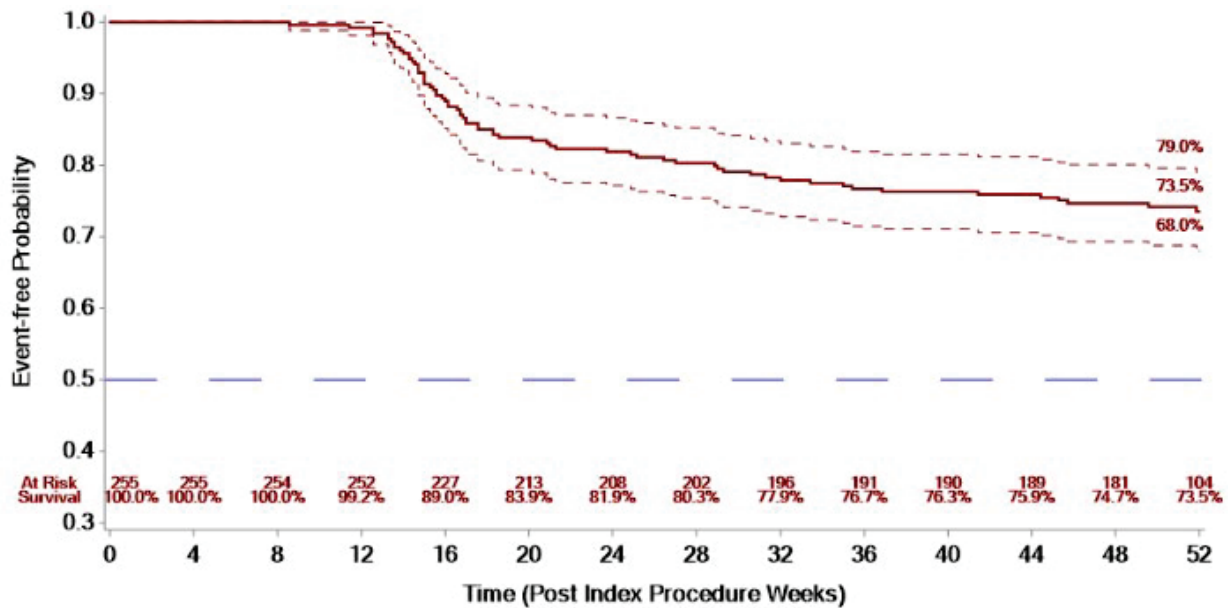
*12-Month Single Procedure Treatment Success*

The 12-Month single procedure success rate was 86.1% (Figure 5) in the Pivotal Main Phase Per-Protocol analysis set. Similar results were reported for the mITT analysis set.



**Figure 5: Kaplan-Meier Analysis of Single Procedure Treatment Success (Pivotal Main Phase Per Protocol Analysis Set, N = 255)**

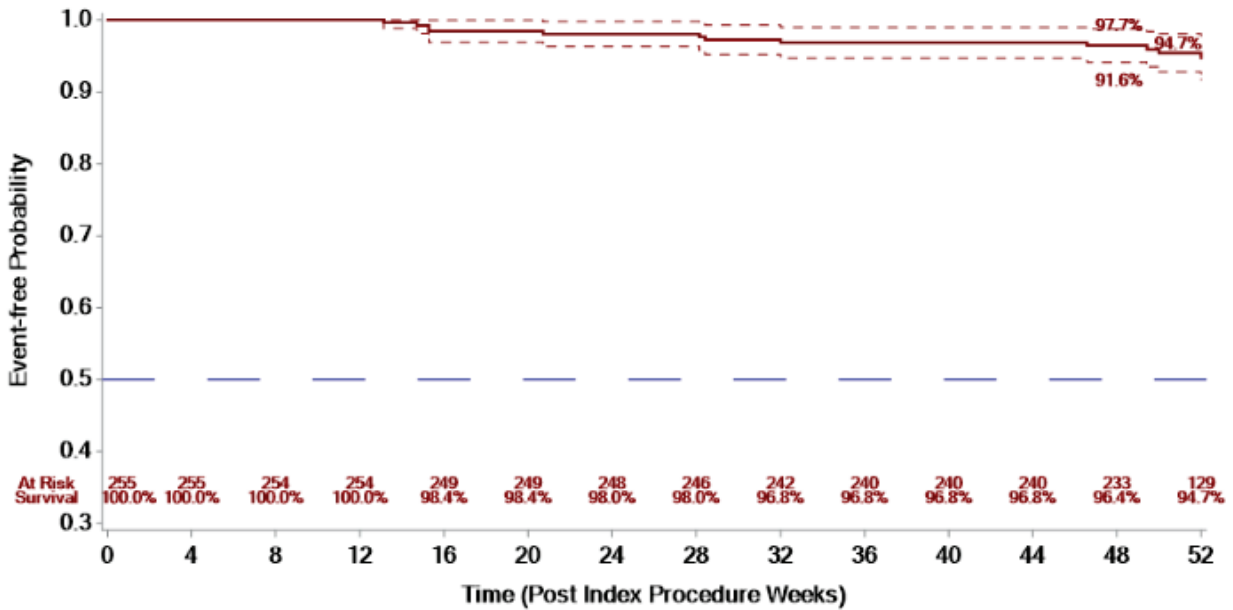
An ad hoc analysis was performed to assess the 12-Month single procedure success, also counting asymptomatic recurrences in the effectiveness evaluation period as failures. As shown in Figure 6 below, the 12-month single procedure success rate taking both asymptomatic and symptomatic recurrences into account was 73.5% in the Pivotal Main Phase Per Protocol analysis set. Similar results were reported for the mITT analysis set.



**Figure 6: Kaplan-Meier Analysis of Modified Single Procedure Treatment Success (Pivotal Main Phase Per Protocol Analysis Set, N = 255)**

### Clinical Success

Kaplan-Meier estimates (Figure 7) used to characterize the time to first documented symptomatic atrial tachyarrhythmia episodes based on electrocardiographic data ( $\geq 30$  seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period (Day 91-Day 365) in the Pivotal Main Phase Per Protocol analysis set. The categorization of “symptomatic vs. asymptomatic” was documented based on subject-reported outcomes. The 12-month clinical success was 94.7% (95% CI: 91.6%, 97.7%) in the Per Protocol analysis set.



**Figure 7: Kaplan-Meier Analysis of Clinical Success (Pivotal Main Phase, Per Protocol Analysis Set, N=255)**

### Study Conclusion

The results of the AdmIRE pivotal study demonstrated the safety and effectiveness of the VARIPULSE™ Catheter System for PV isolation to treat patients with symptomatic drug-refractory PAF.

### 3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with safety and effectiveness outcomes. The study was not specifically powered for sex, age, or race subgroups.

**Table 20: Primary Safety Endpoint by Sex**

Pivotal Main Phase	Primary Safety Endpoint	Male	Female
mITT Analysis Set (N=274)	n/N	2/174	6/98
	% <sup>[1]</sup>	1.1%	6.1%
Safety Analysis Set (N=277)	n/N	2/176	6/99
	% <sup>[1]</sup>	1.1%	6.1%

[1] The percentage of subjects with PAEs within each sex group. Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

**Table 21: Primary Effectiveness Endpoint by Sex**

Pivotal Main Phase	Primary Effectiveness Success	Male	Female
Per Protocol Analysis Set (N=255)	n/N	122/156	61/90
	% <sup>[1]</sup>	78.2%	67.8%

[1] The percentage of subjects with primary effectiveness success within each sex group. N represents subjects within each group who 1) experienced any failure, 2) completed the 12-month follow-up, and/or 3) had ECG, CEM, or HM data beyond 335 days after index procedure in this analysis.

**Table 22: Primary Safety Endpoint by Age**

Pivotal Main Phase	Primary Safety Endpoint	Age ≥ 65	Age < 65
mITT Analysis Set (N=274)	n/N	5/130	3/142
	% <sup>[1]</sup>	3.8%	2.1%
Safety Analysis Set (N=277)	n/N	5/132	3/143
	% <sup>[1]</sup>	3.8%	2.1%

[1] The percentage of subjects with PAEs within each age group. Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

**Table 23: Primary Effectiveness Endpoint by Age**

Pivotal Main Phase	Primary Effectiveness Success	Age ≥ 65	Age < 65
Per Protocol Analysis Set (N=255)	n/N	101/123	82/123
	% <sup>[1]</sup>	82.1%	66.7%

[1] The percentage of subjects with primary effectiveness success within each age group. N represents subjects within each group who 1) experienced any failure, 2) completed the 12-month follow-up, and/or 3) had ECG, CEM, or HM data beyond 335 days after index procedure in this analysis.

**Table 24: Primary Safety Endpoint by CHA2DS2-VASc Score**

Pivotal Main Phase	Primary Safety Endpoint	Score ≤ 2	Score > 2
mITT Analysis Set (N=274)	n/N	5/201	3/71
	% <sup>[1]</sup>	2.5%	4.2%
Safety Analysis Set (N=277)	n/N	5/203	3/72
	% <sup>[1]</sup>	2.5%	4.2%

[1] The percentage of subjects with PAEs within each group. Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

**Table 25: Primary Effectiveness Endpoint by CHA2DS2-VASc Score**

Pivotal Main Phase	Primary Effectiveness Success	Score ≤ 2	Score > 2
Per Protocol Analysis Set (N=255)	n/N	147/181	36/65
	% <sup>[1]</sup>	81.2%	55.4%

[1] The percentage of subjects with primary effectiveness success within each group. N represents subjects within each group who 1) experienced any failure, 2) completed the 12-month follow-up, and/or 3) had ECG, CEM, or HM data beyond 335 days after index procedure in this analysis.

**Table 26: Primary Safety Endpoint by Race**

Pivotal Main Phase	Primary Safety Endpoint	White	Non-White	Not Reported
mITT Analysis Set (N=274)	n/N	8/224	0/24	0/24
	% <sup>[1]</sup>	3.6%	0.0%	0.0%
Safety Analysis Set (N=277)	n/N	8/226	0/24	0/25
	% <sup>[1]</sup>	3.5%	0.0%	0.0%

[1] The percentage of subjects with PAEs within each group. Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

**Table 27: Primary Effectiveness Endpoint by Race (Per Protocol Analysis Set (N=255))**

Primary Effectiveness Success	White	Asian	Black or African American	American Indian/Alaskan Native	Other	Not Reported
n/N	147/203	11/11	4/6	3/3	1/1	17/22
% <sup>[1]</sup>	72.4%	100.0%	66.7%	100.0%	100.0%	77.3%

[1] The percentage of subjects with primary effectiveness success within each group. N represents subjects within each group who 1) experienced any failure, 2) completed the 12-month follow-up, and/or 3) had ECG, CEM, or HM data beyond 335 days after index procedure in this analysis.

**Table 28: Primary Safety Endpoint by Operator Experience**

Pivotal Main Phase	Primary Safety Endpoint	Low <sup>[2]</sup>	High <sup>[3]</sup>
mITT Analysis Set (N=274)	n/N	4/137	4/135
	% <sup>[1]</sup>	2.9%	3.0%
Safety Analysis Set (N=277)	n/N	4/138	4/137
	% <sup>[1]</sup>	2.9%	2.9%

[1] The percentage of subjects with PAEs within each group. Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

[2] Physicians with no PFA experience.

[3] Physicians with any PFA experience, including physicians who were investigators in InspIRE, had preclinical BW PFA experience or experience with non-BW PFA technology.

**Table 29: Primary Effectiveness Endpoint by Operator Experience**

Pivotal Main Phase	Primary Effectiveness Success	Low <sup>[2]</sup>	High <sup>[3]</sup>
Per Protocol Analysis Set (N=255)	n/N	90/130	93/116
	% <sup>[1]</sup>	69.2%	80.2%

[1] The percentage of subjects with primary effectiveness success within each group. N represents subjects within each group who 1) experienced any failure, 2) completed the 12-month follow-up, and/or 3) had ECG, CEM, or HM data beyond 335 days after index procedure in this analysis.

[2] Physicians with no PFA experience.

[3] Physicians with any PFA experience, including physicians who performed ablations in InspiRE or had PFA experience preclinically or with competitor technology.

#### 4. Pediatric Extrapolation

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

### XI. 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 65 investigators of which none were full-time or part-time employees of the sponsor and 4 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: 4
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

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.

### XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Data from the OUS clinical study titled, “A Study for Treatment of Paroxysmal Atrial Fibrillation (PAF) by Pulsed Field Ablation (PFA) System With Irreversible Electroporation (IRE) (inspire),” were used to support the safety of the VARIPULSE Platform with respect to neurovascular injury (including asymptomatic cerebral emboli (ACE) and asymptomatic cerebral lesions (ACL)), PV stenosis, and esophageal injury. Wave I of the inspire study enrolled 45 subjects who underwent additional neurological,

PV, and esophageal assessments. Of the 40 subjects who underwent magnetic resonance imaging (MRI), 8 presented with ACL, with all lesions resolving by the 1-month cerebral MRI. No subjects presented with esophageal lesions or severe PV stenosis at the 3-month follow-up imaging.

### **XIII. 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 System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

### **XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES**

#### **A. Effectiveness Conclusions**

The pivotal AdmIRE study met its pre-defined performance goal of 50% freedom from recurrence of AF, AT, and AFL measured at 12 months after the index procedure. The performance goal aligns with the recommended minimum chronic acceptable success rate for paroxysmal AF at 12-month follow-up from the, “2017 HRS/EHRA/ECAS/APQRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation,” as well as the performance goals used to evaluate devices with similar indications (e.g., the PULSED-AF study conducted to support P230017). All subjects met the acute effectiveness endpoint (i.e., confirmation of entrance block in all PVs). Of the subjects who experienced a failure associated with recurrence of an atrial tachyarrhythmia (60), 47 (78.3%) experienced AF recurrence, 11 (18.3%) experienced AFL recurrence, and 2 (0.03%) experience AT recurrence. Three subjects met the criteria for AAD failure due to initiation of a new AAD after the index procedure. The secondary effectiveness endpoint on quality of life indicated a clinically meaningful difference in AFEQT scores from baseline following the index procedure.

#### **B. Safety Conclusions**

The pivotal AdmIRE study met its pre-defined performance goal of 12% freedom from PAE. Eight subjects experienced PAEs, including cardiac tamponade (3 events), major vascular access complication/bleeding (2), pericarditis (1), stroke/cerebrovascular accident (2), and transient ischemic attack (1). Additional serious non-primary adverse events occurred and were evaluated for relatedness to the study devices and procedure. One subject experienced cardiac arrest during the procedure following ablation of the left superior pulmonary vein (LSPV), requiring cardiopulmonary resuscitation (CPR) and rescue pacing. The patient recovered during the procedure and was discharged without event. One roll-in subject died following an out-of-hospital cardiac arrest on day 39 post-procedure that was determined to be not related to the study devices or procedure.

### **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 benefits include freedom from atrial fibrillation and other atrial tachyarrhythmias at a likelihood determined to be acceptable by the clinical community. Additional benefits include likely improvement in quality of life. The rate of adverse events was lower than the pre-defined performance goal. No instances of esophageal perforating complications (e.g., atri-esophageal fistula), phrenic nerve injury, major PV stenosis, or renal failure were observed.

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 risks include those associated with any electrophysiology catheterization procedure (e.g., access site complications) and those specific to the ablation modality (e.g., cardiac arrest following application of PF energy).

Additional factors to be considered in determining probable risks and benefits for the VARIPULSE Platform included: (1) the lack of a concurrent control arm in the AdmIRE study and (2) the lack of continuous electrocardiographic monitoring leading to sub-optimal compliance with rhythm monitoring strategies.

#### **1. Patient Perspective**

This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the treatment of drug-refractory, recurrent, symptomatic, paroxysmal AF, 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 instructions for use.

## **XV. CDRH DECISION**

CDRH issued an approval order on November 6, 2024. The final clinical conditions of approval cited in the approval order are below.

1. The Long-Term Safety and Effectiveness Evaluation of the VARIPULSE™ System for the Treatment of Symptomatic - Paroxysmal Atrial Fibrillation (VP PAS) is a prospective, multi-center, non-randomized, observational study to evaluate the long-term effectiveness and safety of the VARIPULSE Catheter System for the treatment

of symptomatic, drug-refractory, paroxysmal atrial fibrillation (PAF). Approximately 250 evaluable adult patients who intend to undergo their de novo pulmonary vein isolation procedure using the VARIPULSE Catheter System to treat symptomatic paroxysmal atrial fibrillation (AF) refractory, intolerant, or contraindicated to at least one Class I or III antiarrhythmic medication will be enrolled and ablated using the VARIPULSE Catheter System, with at least 50% patients being women. The study will include a diverse (i.e., race, ethnicity, gender) patient population. A 12-lead electrocardiogram (ECG) and transthoracic echocardiogram will be performed at baseline and 12 months post-ablation in all patients. A transthoracic echocardiogram (TTE) will be performed in at least 40 subjects and will be collected from any patient who undergoes TTE within 3 months of the 12-month follow-up visit. A 24-hour Holter or equivalent rhythm monitoring will be performed at the 6, 12, 24, and 36 months follow-up evaluations. Follow up clinical data will be collected at discharge, 10-12 weeks, 6-, 12-, 24-, and 36-months post-ablation.

The primary objectives of the VP PAS will be the following:

- 1) Estimating the rate of major procedural complications.
- 2) Estimating the 36-month freedom from documented (symptomatic and asymptomatic) AF, atrial flutter (AFL), or atrial tachycardia (AT) episodes following ablation procedure using the VARIPULSE Catheter System.

Additional Endpoints will include but not limited to the following:

Additional Safety Endpoints:

- 1) Estimating the rate of the following procedure- and/or device-related safety events:
  - a. Cardiac tamponade/perforation in women undergoing paroxysmal AF ablation using the VARIPULSE Catheter System.
  - b. Early mortality after ablation using the VARIPULSE Catheter System through 3 months post-procedure.
  - c. Cardiac arrest that occurs after the AF ablation procedure using the VARIPULSE Catheter System.
  - d. Renal failure through 30 days post-procedure.
- 2) Estimating the rate of serious device or serious procedure related adverse events for catheter ablation using the VARIPULSE Catheter System through 12 months post-procedure.
- 3) Estimating the rate of new ventricular wall motion abnormality seen on echocardiogram at 12 months post-ablation.

- 4) Estimating the rate of major procedural complications in patients of 65 years of age or older.
- 5) Estimating the rate of major procedural complications in women undergoing paroxysmal AF ablation using the VARIPULSE Catheter System.

Additional Effectiveness Endpoints:

- 1) Estimating the rate of acute effectiveness success.
- 2) Estimating 12-month and 24-month freedom from documented (symptomatic and asymptomatic) AF, atrial flutter (AFL), or atrial tachycardia (AT) episodes following ablation procedure using the VARIPULSE Catheter System.
- 3) Estimating 36-month freedom from symptomatic AF, AFL, or AT recurrence following ablation procedure using the VARIPULSE Catheter System.
- 4) Estimating freedom from documented (symptomatic and asymptomatic) AF, AFL or AT episodes off Class I and III antiarrhythmic medications at 12, 24, and 36 months following ablation procedure using the VARIPULSE System.
- 5) Characterizing procedural data, including but not limited to procedure time, fluoroscopy time, number of pulsed field (PF) applications, fluid delivered through the VARIPULSE catheter, and ablation strategy.

You are also required to report any early mortality (through 3 months post-procedure) and any cardiac arrest that occurs after the AF ablation procedure using the VARIPULSE Catheter System within 10 days after you first receive notice of the event.

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

## **XVI. 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.

## **XVII. REFERENCES**

N/A