SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Catheter, percutaneous, cardiac ablation, intended for treatment of atrial fibrillation Generator, Irrigation pump and accessories
Device Trade Name:	DiamondTemp™ Ablation System DiamondTemp™ Ablation Catheter (Models CEDT100S, CEDT200L, CEDTB300S, CEDTB400L) DiamondTemp™ RF Generator (Model CEDTG200) DiamondTemp™ Irrigation Pump (Model CEDTP100) DiamondTemp™ Irrigation Tubing Set (Model CEDTTS100) DiamondTemp™ Catheter-to-RF Generator Cable (Model CEDTC100) DiamondTemp™ GenConnect Cable (Model CEDTGC100) DiamondTemp™ EGM Cable (Model CEDTEGM100)
Device Procode:	OAE
Applicant's Name and Address:	Medtronic Inc. 8200 Coral Sea Street NE Mounds View, MN 55112 USA
Date(s) of Panel Recommendation:	None

Premarket Approval Application

(PMA) Number: P200028

Date of FDA Notice of Approval: January 28 2021

II. INDICATIONS FOR USE

The DiamondTemp Catheter is indicated for use in cardiac electrophysiological mapping (stimulation and recording) and for treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation when used in conjunction with the DiamondTemp RF Generator and accessories (DiamondTemp Catheter-to-RF Generator Cable, DiamondTemp GenConnect Cable, DiamondTemp EGM Cable, DiamondTemp Irrigation Pump, DiamondTemp Irrigation Tubing Set) and compatible mapping system.

III. CONTRAINDICATIONS

The DiamondTemp Catheter is contraindicated for use in:

- Patients with active systemic infection;
- Patients with prosthetic valves;
- Patients with intracardiac thrombus or myxoma, or interatrial baffle or patch via transseptal approach;
- Patients unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation;
- Pregnant women and children <18 years of age;
- Patients who are hemodynamically unstable

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the individual DiamondTemp Ablation Catheter (Unidirectional/Bidirectional), DiamondTemp RF Generator, DiamondTemp Irrigation Pump, DiamondTemp Catheter-to-RF Generator Cable, DiamondTemp GenConnect Cable, DiamondTemp EGM Cable, and DiamondTemp Irrigation Tubing Set labeling.

V. DEVICE DESCRIPTION

The DiamondTemp Ablation System includes the DiamondTemp Ablation Catheter (Unidirectional/Bidirectional), DiamondTemp RF Generator, DiamondTemp Irrigation Pump, DiamondTemp Catheter-to-RF Generator Cable, DiamondTemp GenConnect Cable, DiamondTemp EGM Cable and DiamondTemp Irrigation Tubing Set. The DiamondTemp Ablation System is designed to deliver radiofrequency (RF) energy to the cardiac anatomy via

the DiamondTemp Catheter. **Figure 1** shows the DiamondTemp System when connected to a compatible mapping system.

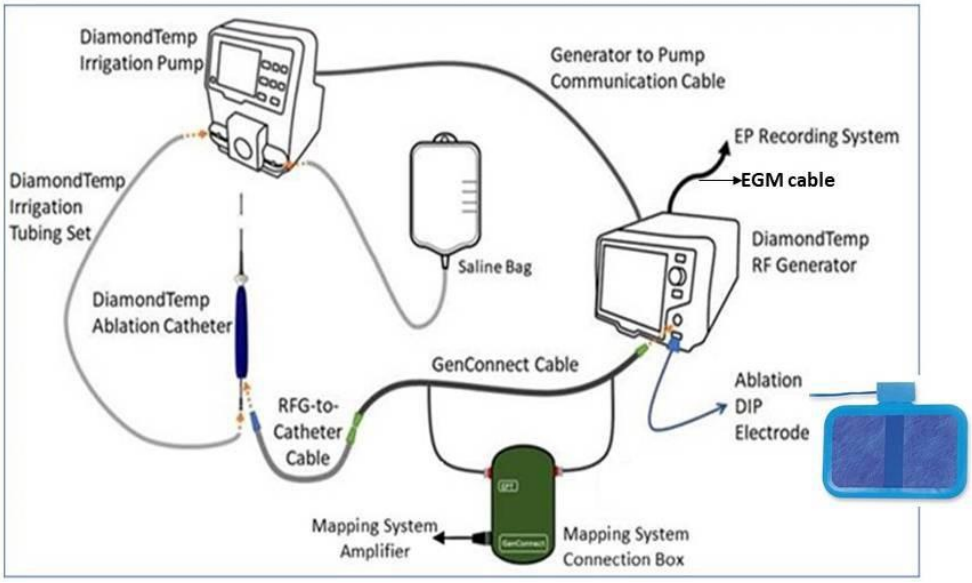


Figure 1. DiamondTemp Ablation System

The DiamondTemp ablation catheter is a 7.5Fr ablation tip quadripolar open-irrigated ablation catheter designed to deliver radiofrequency (RF) energy for cardiac ablation. The catheter is available with unidirectional or bidirectional steering and either small curve or large curve reach (Refer to **Table 1** for model information).

Table 1. Catheter models and specifications

Catheter shaft size (outer diameter)	2.83mm (8.5 Fr)
Catheter ablation tip size	2.50 mm (7.5 Fr)
Length (nominal)	110 cm (43.3 in)
Model	**Description**
CEDT100S	Unidirectional, small curve (45 mm)
CEDT200L	Unidirectional, large curve (63 mm)
CEDTB300S	Bidirectional, small curve (45 mm)
CEDTB400L	Bidirectional, large curve (63 mm)

The catheter tip includes diamonds to enable rapid cooling and thermocouples for temperature sensing during RF ablation.

The catheter, when connected to the tubing set and irrigation pump, delivers normal

saline via a lumen and ports in the catheter tip to provide cooling of the catheter tip and tip-tissue interface. One luer connection at the proximal end of the handle connects to the tubing set, allowing the irrigation pump to generate the flow of normal saline to the catheter.

The DiamondTemp RF generator provides RF energy and temperature monitoring functions, as well as control and communication to the DiamondTemp irrigation pump and commercially available external devices, such as cardiac stimulators, electrophysiology recording systems, and compatible EP navigational and mapping systems.

The generator operates in temperature control mode. The desired catheter tip-to-tissue temperature is selected by the user. Thermocouples in the catheter tip provide temperature feedback and the generator automatically adjusts the power output to maintain the desired tip-to-tissue temperature.

The generator (**Figure 2**) has a touch-screen display, control buttons, and a control knob for modifying and controlling ablation parameters during the procedure. Ablation parameters such as temperature, power, impedance, duration, and irrigation flow rate are displayed on the front panel and can me recorded and saved by the generator in a format that can be downloaded to a computer or a USB flash drive.

A footswitch is also included with the generator and may be used as an option to start or stop RF energy delivery.

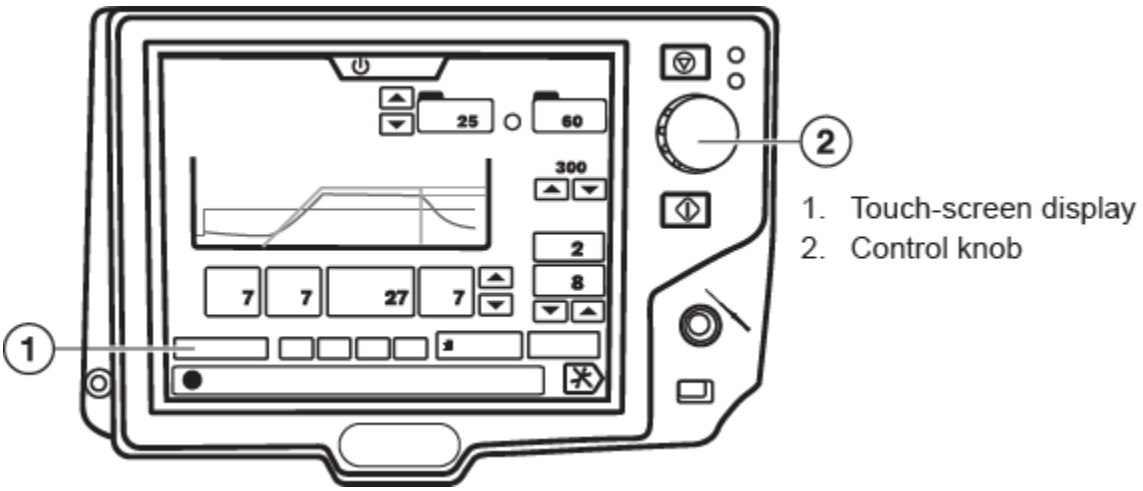


Figure 2. DiamondTemp RF Generator

The DiamondTemp irrigation pump (**Figure 3**) delivers saline to the catheter when used in conjunction with the DiamondTemp tubing set. The irrigation pump has a touch screen display and flow control button that controls a two-flow-rate feature for easy selection of the appropriate irrigation flow rate. The rate can be changed between a low flow rate (1-5 mL/min) and a high flow rate (6-30 mL/min). Large numbers on the touch screen display and an LED light on the flow control button indicate the flow rate selected. The irrigation pump communicates with the DiamondTemp generator and may be operated independently or under control of the generator

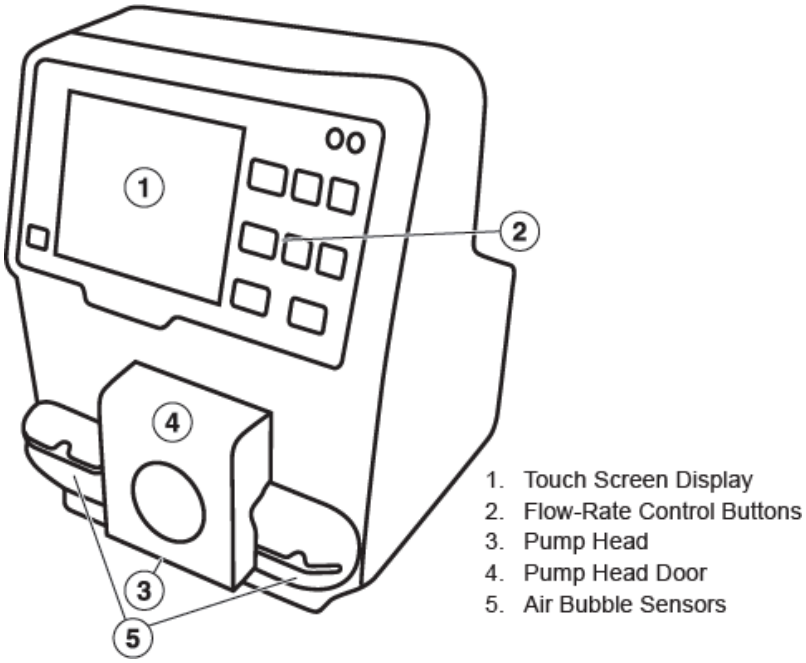


Figure 3. Epix Therapeutics Irrigation Pump

A transparent pump head door (4, **Figure 3**) protects the rotating pump head (3, **Figure 3**), while allowing visibility of the entire tubing set during pump operation.

The tubing set is placed in the path and around the pump head for operation. The irrigation pump uses twin ultrasonic air bubble detectors (5, **Figure 3**) for added safety in preventing air infusion.

Audible or visual indicators and informational messages displayed on the touch-screen panel (1, **Figure 3**) warn of air in the tubing, an open pump head door, or other operational conditions.

The DiamondTemp irrigation tubing set consists of the following components (**Figure 4**). The length of the tubing set assembly is 3.66 m (144 in).

- A drip chamber with an intravenous (IV) spike for connection to an IV bag
- A pump head section with plastic retention clips that fit the slots for the air-bubble detectors (located inside the irrigation pump)
- A catheter end that terminates in a standard luer lock connector and connects to
- the DiamondTemp ablation catheter
- A 3-way stopcock (not shown)

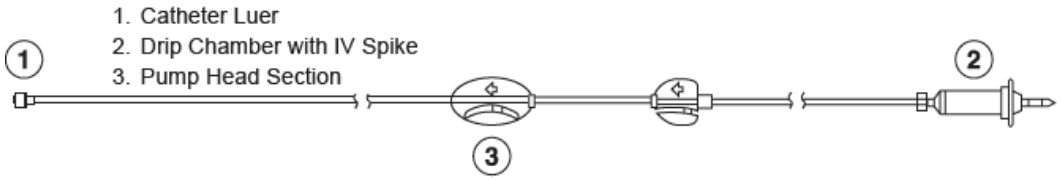


Figure 4. Tubing Set Components

The DiamondTemp Catheter-to-RF Generator (RFG) cable is used to connect the DiamondTemp catheter to the RF generator. The distal end of the cable has a 19-pin connector that connects tothe DiamondTemp catheter. The proximal end of the cable has a 26-pin connector that
connects to the RF generator. The length of the cable is 2.5 m (8.2 ft).

The DiamondTemp GenConnect cable connects the DiamondTemp catheter to the DiamondTemp RF generator when a GenConnect device is used. The distal end of the GenConnect cable has a 26-pin female connector that connects to the catheter cable and the proximal end has a 26-pin male connector that connects to the generator. The length of the cable is 1.8 m (6.0 ft).

The DiamondTemp EGM Cable connects the RF generator to a hospital's compatible EP recording system. This Cable is used only with the DiamondTemp ablation system. The DiamondTemp EGM Cable is 3 meters (m) long and has 4 connectors. The one end of the Cable has a male, 9-pin connector that will connect with the DiamondTemp RF Generator and the other end of the Cable has male, 2.0 mm shrouded pin connectors (x4) that will connect with the hospital's compatible EP recording system. The DiamondTemp EGM Cable is provided non-sterile.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation, including:

- Commercially available PMA-approved ablation devices

- Pharmacological therapy for rate and/or rhythm control
- Electrical or pharmacologic cardioversion
- Surgical intervention to create atrial lesions
- Implantable devices to control heart rate.

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 DiamondTemp Ablation System has been marketed in select European countries (Belgium, Germany, Spain, Italy, France and United Kingdom) for ablation of cardiac arrhythmias. In Australia, the system received approval in 2019 but has not yet begun distribution.

There have been no product withdrawals from any country for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events (e.g., complications) associated with the use of the system during cardiac ablation therapy to treat arrhythmias include the following

- Abnormal vision
- Air embolism
- Anaphylaxis
- Anemia
- Aneurysm
- Angina
- Arrhythmia (including new or worsening of existing condition, or requiring cardioversion)
- Arterial or venous thrombus
- Atrial septal defect
- AV fistula
- Cardiac arrest
- Cardiac tamponade
- Catheter entrapment leading to valve or heart wall damage
- Catheter insertion site hematoma
- Chest pain (non-specific)
- Congestive heart failure exacerbation

- Component damage to ICD or pacemaker
- Coronary artery dissection
- Death
- Dislodgement of implantable device or permanent pacing lead
- Dizziness
- Embolic events, including infarction of other tissues, coronary, pulmonary, and bowel structures
- Endocarditis
- Esophageal damage or necrosis
- Exacerbation of COPD
- Exacerbation of pre-existing atrial fibrillation
- Fluid overload
- Gastroparesis or GI event
- Hemorrhage
- Hemothorax
- Hypotension
- Hypoxia
- Inadvertent AV block
- Infection
- Myocardial infarction
- Neck, back, or groin pain
- Palpitations
- Perforation (cardiac)
- Pericardial effusion
- Pericarditis
- Peripheral venous thrombosis
- Phrenic nerve damage
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary vein stenosis
- Radiation injury resulting in dermatitis, erythema, etc.
- Renal insufficiency or failure
- Respiratory failure
- Seizure
- Sepsis
- Skin burns
- Stroke or cerebrovascular incident

- Syncope
- Thromboembolic event
- Transient ischemic attack
- Vasovagal reaction
- Ventricular arrhythmia
- Vessel wall or valvular damage or insufficiency

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

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical testing of DiamondTemp Ablation System included verification and validation (device, system, and software), biocompatibility of patient-contacting materials, sterilization, packaging, and shelf life testing, and animal studies. Performance testing was conducted to demonstrate design integrity. Tests that were identified in standards or guidance documents were performed based on product specification requirements. The following summarized testing was performed on devices representative of proposed commercial devices manufactured by trained operators. "Pass" denotes the devices and systems met established product specification and/or performance criteria, or were in conformance with the requirements of the standards tested to. Test results confirmed that the DiamondTemp Ablation System met product specifications.

A. Laboratory Studies

The DiamondTemp Ablation Catheter passed design verification (functional) bench testing including dimensional, strength, reliability, mechanical, and electrical integrity. Testing including performance of the DiamondTemp RF Generator used in conjunction with the DiamondTemp Catheter and all other system components, which include the DiamondTemp Irrigation Pump and Tubing Set.

Table 2 below summarizes the bench testing for the Bidirectional and Unidirectional Catheters. This includes reliability, mechanical and electrical integrity and performance test results.

Table 2: Design Verification Testing of DiamondTemp Ablation Catheters (Unidirectional and Bidirectional)

Test	Acceptance Criteria	Results
Dimensional: Tip Size, Tip Length, Shaft Size, Ring Size, Effective Catheter Length, Distal Small/Large Curve	All physical dimensions identified in the product specifications must be met.	Pass

Interface – connector cycling	After 10 engagement/disengagement cycles: - the catheter shall have no physical or mechanical failure from the handle - the engagement and disengagement forces of the catheter shall be ≤ 20.0lbf (89N) - when the catheter is straight, tip electrode (D1, D2) resistance shall be 4.4 Ω ± 15%. - when the catheter is straight, ring (R1,R2) electrode resistance shall be 4.4 Ω ± 20% - when the catheter is straight, thermocouple resistance shall be 144 Ω ±10% at room temperature - when the catheter is straight, there shall be no wire-to-wire shorting. The DC resistance > 5MΩ - when the catheter is straight, there shall be no electrical opens	Pass
Introduction/Withdrawal – Mechanical Integrity	After 20 introduction/withdrawal cycles using a commercially available short sheath 8.5 F (2.67 mm), there shall be no mechanical failures such as bending, bond delamination, electrode movement, or adhesive dislodgment.	Pass
Introduction/Withdrawal – Thermal Shock Conditioning	At the end of 5 thermal/shock cycles and then 20 introduction/withdrawal cycles using a commercially available short sheath 8.5 F (2.67 mm), there shall be no mechanical failures such as bending, bond delamination, electrode movement, or adhesive dislodgment.	Pass
Introduction/Withdrawal – Electrical Integrity	After 10 introduction/withdrawal cycles using a commercially available short sheath 8.5 F (2.67 mm): -Tip, Ring, Thermocouples meet electrical requirements - no electrical opens	Pass
Steering Mechanism Acutuation – Unidirectional or Bidirectional	For unidirectional catheter - the catheter shall deflect in one direction. For bidirectional catheter – the catheter shall deflect in two directions.	Pass
Steering Life Cycle	After 100 steering cycles around a 4.0” diameter: - catheter curves shall meet its post-sterile curve template - catheter shall be removed from a commercially available steerable sheath	

	- no bond failures, component malfunctions, or separations from catheter body - tip electrode (D1, D2) resistance shall be 4.4 Ω ± 15% - ring (R1,R2) electrode resistance shall be 4.4 Ω ± 20% - thermocouple resistance shall be 144 Ω ±10% at room temperature - DC resistance > 5MΩ	
Twisting Reliability	After two 360◦ twist rotations: - the catheter tip shall not separate from the catheter body; the butt bond shall not separate. - tip electrode (D1, D2) resistance shall be 4.4 Ω ± 15%. - ring (R1,R2) electrode resistance shall be 4.4 Ω ± 20% - thermocouple resistance shall be 144 Ω ±10% at room temperature - DC resistance > 5MΩ - no electrical opens After one 90◦ rotation, the cooling extension tubing shall have no physical or mechanical failure (external components only)	
Tensile strength	The Tensile strength of catheter joints shall be less than the defined maximum values per requirements documentation on each joint or juncture.	Pass
Curve degradation	The catheter shall meet its post-sterile curve template after simulated use.	Pass
Torque response	Torsional transmission along the catheter shaft shall be >1.22ozf-in	Pass
Curve range	Catheter shall fully deflect in two directions after use and knob shall operate appropriately.	Pass
Distal Bending Stiffness	Bending stiffness of the catheter shaft shall be < 50gf.	Pass
Distal Buckling	The catheter shaft shall buckle at < 272gf	Pass
Cooling Extension Tubing Integrity	After one 90° rotation the cooling extension tubing shall have no physical or mechanical failures.	Pass
Holding Pressure Integrity	The catheter shall hold 45psi for at least 30sec with $\Delta P \leq 2$ psi when the irrigation	Pass

	holes are plugged, both normal and after 100 steering cycles and around a 4in diameter.	
Head Pressure Integrity	The maximum head pressure shall be less than 20psig at 8ml/min for 1 min without compromising the cooling system, both normal and after 100 steering cycles and around a 4in diameter.	Pass
Thermal Response Time	Thermal response time of the thermocouple shall be ≤ required seconds per product requirements.	Pass
Temperature Accuracy	Thermocouple accuracy shall be met in the range 37°C - 70°C.	Pass
Corrosion	The catheter shall not exhibit any corrosion when tested in accordance with ISO 10555-1.	Pass
Energy Delivery: RF Functionality	The catheter with cable shall withstand an operating power of 50W.	Pass
Unintended Energy Delivery: RF Leakage Current	The leakage current shall be less than the limit calculated at the time of the test, per EN 60601-2-2.	Pass
Unintended Energy Delivery: High-Frequency Dielectric Strength	The dielectric strength shall withstand 120% of the maximum output voltage of the generator, when the generator is set to 50W.	Pass
Unintended Energy Delivery: Mains-Frequency Dielectric Breakdown Voltage	The catheter shaft dielectric strength shall withstand ablation operational voltages (max 500Vp / 60Hz).	Pass

Table 3 below summarizes the verification testing for the DiamondTemp Irrigation and Tubing Set.

Table 3: DiamondTemp Irrigation Pump and Tubing Set Design Verification Testing

Test	**Acceptance Criteria**	**Results**
Dimensions, connections and labeling	All physical dimensions, connections and labeling identified in the product specifications must be met.	Pass
Acoustic output limit	Acoustic level < 83 dBA	Pass
Mains power requirements including	Mains current < 5A	Pass
Software control of pump flow rates	Interface between microprocessor and motor controller processor	Pass
Air bubble detection	Bubble detection at various flow rates	Pass

Flow Performance - Flow rate range, Back Pressure, Air purge flow rate, Flow rate operating duty life cycle and life time	Flow rate range, accuracy and tolerances at 1, 3, 5, 8, 15, 30, and 60mL/min; Specified flow rate verified into a back pressure up to 45psi	Pass

Software Validation

The DiamondTemp RF Generator firmware (Version 1.30US) and DiamondTemp Irrigation Pump firmware (Version 1.20) have primary responsibility for the operator interface, procedure settings, control of RF power of the DiamondTemp RF Generator, and saline irrigation for the DiamondTemp Irrigation Pump. The DiamondTemp Irrigation Pump firmware also communicates with the DiamondTemp RF Generator to react to the ablation state of the generator. When used with the DiamondTemp Ablation Catheters, the generator operates in temperature-control mode in order to maintain the defined temperature input. The generator computes and displays data related to its operation and the procedure and interfaces with all other peripheral equipment.

Firmware testing included a full suite of safety and performance tests. The firmware was evaluated through unit, integration, verification and validation testing to demonstrate that the performance and safety of the DiamondTemp RF Generator and the DiamondTemp Irrigation Pump conform to specifications.

Accessories

Additional design verification and validation (bench) testing was completed for the DiamondTemp Ablation System, which includes the DiamondTemp RF Generator, DiamondTemp Irrigation Pump, DiamondTemp Tubing Set, DiamondTemp Catheter-to-RFG Cable, EGM cable, and DiamondTemp GenConnect Cable. Testing includes electrical safety, electromagnetic compatibility (EMC), system design validation testing and system usability testing.

The DiamondTemp Catheter-to-RFG Cable and GenConnect Cable bench testing includes functionality after ten (10) cycles of cleaning for the Catheter-to-RFG Cable and (1) cycle of cleaning for the GenConnect Cable, functionality after ten (10) cycles of autoclave sterilization (Catheter-to-RFG Cable only), life cycle flexibility, connector tensile strength, mechanical connection force, connector reliability, and conformance to resistance, impedance, capacitance, and isolation resistance requirements.

Biocompatibility

Biocompatibility testing of the DiamondTemp Ablation Catheter (Unidirectional/ Bidirectional) and the DiamondTemp Irrigation Tubing Set was conducted in accordance with ISO 10993-1:2009 - Biological evaluation of medical devices – Part 1, and

FDA/CDRH/ODE Blue Book Memorandum G95-1, Use of International Standard ISO-10993.

The DiamondTemp Ablation Catheter test samples are derived from the finished product. The catheter is classified according to ISO 10993-1 as follows:

- Category: Externally Communicating
- Contact Duration: < 24 hours (Limited)
- Device Body Contact: Circulating Blood Path

A summary of the results is provided in **Table 4** below and demonstrates that the DiamondTemp Ablation Catheters are biocompatible per ISO 10993-1. These test results provide objective evidence that the catheter is biocompatible per its intended use.

Table 4. Biocompatibility Testing Summary – DiamondTemp Ablation Catheter (Unidirectional/Bidirectional)

Test Performed / Applicable ISO 10993 Part No.	**Test Performed**	**Results**
Cytotoxicity (10993-5)	MEM Elution, GLP	Pass
Sensitization (10993-10)	ISO Guinea Pig Maximization Sensitization Test, GLP	Pass
Irritation or Intracutaneous Reactivity (10993-10)	ISO Intracutaneous Irritation Test, GLP	Pass
Acute Systemic Toxicity (10993-11)	ISO Acute Systemic Injection Test, GLP	Pass
Material-Mediated Pyrogenicity (10993-11)	ISO Materials Mediated Rabbit Pyrogenicity, GLP	Pass
Hemocompatibility (10993-4)	ASTM Hemolysis, Direct Contact, GLP	Pass
Hemocompatibility (10993-4)	ASTM Hemolysis, Extract Method, GLP	Pass
Hemocompatibility (10993-4)	Complement Activation, GLP	Pass
Hemocompatibility (10993-4)	Thrombogenicity, GLP	Pass
Hemocompatibility (10993-4)	Partial Thromboplastin (PTT) Test, GLP	Pass
Latex	ASTM D6499 Inhibition ELISA	Pass

USP Physicochemical	USP Physicochemical Tests for Plastics, GLP	Pass

Patient contacting materials of the DiamondTemp Ablation Catheters are listed in **Table 5** below.

Table 5: DiamondTemp Ablation Catheter (Unidirectional/Bidirectional) Blood/Fluid Contact Components and Materials

Component	**Material Name**
Tip, Proximal Electrode and Ring Electrode	Platinum/Iridium
Tip, Distal/Proximal Diamond	Chemical Vapor Deposited (CVD) Diamond
Shaft	Pebax 7233, 5533, 4033, 3533
Irrigation Bump Tube	Pebax 7233
Luer	Polycarbonate
Irrigation Tube (Thin Tip)	304 Stainless Steel
Adhesives	Cyanoacrylate, UV Cyanoacrylate, Epoxy, Accelerator
Solder/flux	Tin/Silver/Copper
Distal Thermocouple	Polyimide, Loctitie

The DiamondTemp Irrigation Tubing Set test samples were derived from the finished product. The tubing set is classified according to ISO 10993-1 as follows:

- Category: Externally Communicating
- Contact Duration: < 24 hours (Limited)
- Device Body Contact: Blood Path Indirect

A summary of the results is provided in **Table 6** below and demonstrates that the DiamondTemp Irrigation Tubing Set is biocompatible per ISO 10993-1. These test results provide objective evidence that the catheter is biocompatible per its intended use.

Table 6. Biocompatibility Testing Summary – DiamondTemp Tubing Set

Test Performed / Applicable ISO 10993 Part No.	**Test Performed**	**Results**
Cytotoxicity (10993-5)	MEM Elution, GLP	Pass
Sensitization (10993-10)	ISO Guinea Pig Maximization Sensitization Test, GLP	Pass

Irritation or Intracutaneous Reactivity (10993-10)	ISO Intracutaneous Irritation Test, GLP	Pass
Acute Systemic Toxicity (10993-11)	ISO Acute Systemic Injection Test, GLP	Pass
Material-Mediated Pyrogenicity (10993-11)	ISO Materials Mediated Rabbit Pyrogenicity, GLP	Pass
Hemocompatibility (10993-4)	ASTM Hemolysis, Direct Contact, GLP	Pass
Hemocompatibility (10993-4)	ASTM Hemolysis, Extract Method, GLP	Pass

Indirect patient contacting materials for the DiamondTemp Irrigation Tubing Set are listed in **Table 7** below.

Table 7: DiamondTemp Irrigation Tubing Set Indirect Blood/Fluid Contact Components and Materials

Component	**Material Name**
Spike, Vented	ABS
Spike Cap, Vented	Polyethylene
Tubing	Tygon, DEHP-free PVC
Drip Chamber	DEHP-free PVC
Adhesives	Cyanoacrylate, UV Loctite
StopCock	Polycarbonate
Luer	PVC

B. Animal Studies

A total of five (5) in vivo animal studies for the DiamondTemp Ablation System were conducted to support paroxysmal atrial fibrillation with the DiamondTemp Ablation Catheter. The purpose of Animal Studies is described as follows.

- Before undertaking a First-in-Man (FIM) clinical evaluation a confirmatory chronic animal study was conducted to characterize the safety profile and performance of the DiamondTemp Ablation System in an animal model and confirm readiness for human use.
- Two (2) confirmatory, comparative GLP animal evaluations were conducted to assess the safety and effectiveness of the DiamondTemp Ablation System prior to initiation of the DIAMOND-AF IDE clinical study. The first study compared the DiamondTemp Ablation System in sub-acute and chronic animal evaluations in a canine model to a commercial control device (ThermoCool Catheter) using two operators. The second study

characterized the DiamondTemp Ablation System performance as well as a commercial control device (ThermoCool Catheter/Stockert Generator) in a perfused swine tissue model ("thigh model") scientifically recognized for characterizing ablation systems.

- A confirmatory, comparative chronic GLP evaluation using three (3) clinical physician operators was undertaken to evaluate safety and effectiveness and to compare handling and performance of the DiamondTemp Ablation System to a commercial control device (TactiCath Quartz Contact Force Catheter).
- As part of design validation for the CEDTG200 Generator, a chronic study in the canine atria was conducted using 2 clinical physician operators was conducted to characterize the safety of the DiamondTemp Ablation System in the creation of atrial endocardial lesions.

A summary of the animal study is provided in **Table 8**.

Table 8: DiamondTemp Ablation System In Vivo Animal Summary

Study Type	**Number of Animals**	**Follow-up Duration**	**Relevant Findings**
Non-GLP Chronic Canine Study	N=4	14 days	A Chronic Study to Assess the Safety and Performance of the DiamondTemp System in the Creation of Endocardial RF Ablation Lesions in the Canine Atria The confirmatory chronic study characterized the safety profile and device performance of the DiamondTemp Ablation System in the creation of endocardial radiofrequency (RF) ablation lesions in the canine atria. The study also demonstrated the compatibility of the DiamondTemp Ablation System with ancillary devices and equipment. No significant physical, neurological, or pathologic abnormalities were observed. The gross anatomical and histo-pathological findings were representative of RF ablation procedures and the analysis of the lesions showed that most lesions created were transmural. No significant safety concerns were raised in the histopathology assessment.
GLP Chronic Canine Study	N=25	7 days (N=12) 30 days (N=13)	A Sub-Acute and Chronic GLP Study to Evaluate the Safety of the DiamondTemp Ablation System in the Creation of Endocardial RF Ablation Lesions in the Canine Atria

			The DiamondTemp Ablation System was compared to the commercially available the ThermoCool/Stockert System approved for the treatment of atrial fibrillation. There were no significant differences regarding adverse events and safety outcomes when the DiamondTemp was compared to the control device. The findings of the health report and clinical pathology and histopathology reports were comparable for both study groups. No incidences of microemboli in up/downstream organs and draining myocardium were reported, no clinically significant collateral injury or lesions were reported, no pulmonary vein stenosis were reported in either study group at any of the termination time points and no cardiac tamponade or perforation were reported. None of the findings were unanticipated. The effectiveness of the DiamondTemp Ablation System was also established with the demonstration of electrical conduction block in 2 pulmonary veins at least 20 minutes after final ablation treatment in the vessel as determined by EGM in all treated animals.
Acute Swine GLP Study	N=4	Acute (same day)	A GLP Study to Compare the Ablation Lesions Created using the DiamondTemp Catheter/Ablation System to the Biosense Webster ThermoCool Catheter/Stockert System in the Swine Thigh Prep Model There were no significant differences in lesion diameter and volume between the DiamondTemp test article for any lesions created under WC operating conditions. The lesion diameter and volumes achieved under IFU operating conditions resulted in smaller lesions for the DiamondTemp Ablation system when compared to the control. There was no significant difference in the incidence rate of steam pops between the DiamondTemp test article and the control test articles in any combination of orientation and ablation settings except the Parallel WC condition. In that condition, the DiamondTemp test article yielded significantly fewer steam pops than the control (4/15, 27% vs. 11/15, 73%; p=0.027). The presence of char on the catheter was not observed after any ablation for either the DiamondTemp or control test articles.

			The presence of thrombus on the catheter or tissue represented a critical endpoint relative to the ability to characterize the safety profile of the DiamondTemp due to the ability of thrombotic material to cause thromboembolic events in critical organs including the ventricular myocardium, the kidneys, the brain or the lungs. For thrombus on the device and tissue, the DiamondTemp was equivalent to the control device at every test condition.
Chronic Canine GLP Study	N=12	30 days	A Chronic GLP Study to Evaluate the Safety of the DiamondTemp System in the Creation of Endocardial RF Ablation Lesions in the Canine Atria. Safety of the DiamondTemp Ablation System (Test Article) was compared to the Abbott/St. Jude TactiCath Quartz Contact Force Control Catheter (Control Article). There was no significant difference in handling and usability scores of the DiamondTemp to the control. There was no occurrence of catheter entrapment, valvular injuries, phrenic nerve injury or pulmonary vein stenosis in the test or control animals. All animals in both the test and control groups showed presence of electrical conduction block in at least two pulmonary veins. DiamondTemp resulted in a significantly shorter total ablation time, due to shorter individual RF delivery times. DiamondTemp also resulted in less fluid delivered during the procedures. The safety and effectiveness criteria of the study were met. The DiamondTemp Ablation System demonstrated safety and effectiveness when compared to a commercial control device. The performance and usability of the DiamondTemp Ablation System was comparable or better than the control device.
Non-GLP Chronic Canine Study	N=6	30 days	A chronic study to characterize the safety of the DiamondTemp Ablation System in the creation of atrial endocardial ablation lesions in the canine model. Multiple focal ablations or drag lesions were applied in three animals each. The findings of the health report and clinical pathology and histopathology reports were acceptable. No incidences of microemboli in up/downstream organs

			and draining myocardium were reported, no clinically significant collateral injury or lesions were reported, no pulmonary vein stenosis were reported in either study group at any of the termination time points and no cardiac tamponade or perforation were reported. The effectiveness of the DiamondTemp Ablation System was established with the demonstration of electrical conduction block in 2 pulmonary veins at least 20 minutes after final ablation treatment in the vessel as determined by EGM in all treated animals.

C. Additional Studies

Sterilization, Packaging, and Shelf Life

The DiamondTemp Ablation Catheters (Unidirectional/Bidirectional),DiamondTemp Irrigation Tubing Set, and DiamondTemp Catheter-to-RFG Cable are supplied sterile, single use and ready to use. The catheters are sterilized via 20% ethylene oxide (EO) and 80% carbon dioxide gas, and the tubing set and catheter-to-RFG cable are sterilized via 100% ethylene oxide (EO) at qualified sterilization facilities using a validated sterilization cycle. The sterilization process validation was conducted to provide a sterility assurance level (SAL) of at least 10^{-6} in accordance with ISO 11135-1:2007, a recognized standard for EO terminally sterilized medical devices.

The DiamondTemp Catheter-to-RFG Cable is provided sterile, not patient-contacting, and can be re-sterilized up to ten (10) times after initial use. The GenConnect cable is not patient-contacting, can be reused multiple times and is not sterilized.

The packaged DiamondTemp Unidirectional and Bidirectional Ablation Catheters, DiamondTemp Catheter-to-RF Generator Cable, DiamondTemp GenConnect Cable, EGM Cable, and DiamondTemp Irrigation Tubing Set were evaluated to demonstrate product and packaging system performance after exposure to applicable conditioning. Device functionality after the following conditioning was assessed:

- Storage / climatic conditioning per ASTMD 4332 for exposure to extreme cold, tropical, and desert temperature and humidity
- Distribution conditioning per ASTM D4169 cycle 13 (variations of vibration, shock, and compression).
- Challenge sterilization of 2x Ethylene Oxide

Packaging System performance testing included maintenance of sterile barrier integrity from gross leaks per ASTM F2096, pouch seal strength tested per ASTM F288, and legibility of labeling and Instructions for Use for the subject devices.

The DiamondTemp Ablation Catheters, DiamondTemp Catheter-to-RFG Cable, and DiamondTemp Irrigation Tubing Set are labeled for 1-year shelf life.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed the DIAMOND-AF Study to establish a reasonable assurance of safety and effectiveness of radiofrequency ablation with the DiamondTemp Ablation System for the treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation in the US under IDE # G170227. 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

Patients were treated between November 6, 2017 and October 26, 2018. The database for this original PMA reflected data collected through December 3, 2019 and included 482 patients. There were 23 investigational sites (14 US sites, 1 Canadian site, and 8 France/Italy/Czech Republic sites).

The study was a prospective, single-blind, 1:1 randomized, controlled, multicenter pivotal clinical trial. The study enrolled subjects with symptomatic paroxysmal atrial fibrillation refractory to one or more antiarrhythmic drugs (Class I-IV). Enrolled subjects were randomized to catheter ablation using the investigational DiamondTemp Ablation System or the control TactiCath Contact Force Ablation Catheter. The control device received FDA approval for the treatment of paroxysmal atrial fibrillation (P130026). Subjects were followed up prior to hospital discharge and at 7 days, 1 month, 3 months, 6 months, and 12 months post-ablation. Subjects were provided a cardiac event monitor at the hospital pre-discharge visit to be used throughout the duration of the study. This data was transmitted to and read at an ECG core lab.

The study success was originally defined by freedom from documented symptomatic atrial fibrillation (AF), atrial flutter (AFL), and atrial tachycardia (AT) recurrence following the blanking period through the end of the effectiveness evaluation period (from 3-month to 12-month follow-up post-ablation procedure) and freedom from Primary Safety Device- or Procedure-related serious adverse events (SAE) composite occurring within 30 days of the AF ablation procedure (or clinically symptomatic pulmonary vein stenosis through 6 months post-index ablation procedure). Prior to data lock, the sponsor and FDA agreed to change the primary effectiveness endpoint to include all-cause atrial arrhythmia recurrence. The study would be considered successful if the investigational device (DiamondTemp Ablation System) is considered non-inferior to the control device for the primary safety and effectiveness endpoints.

An independent ECG Core Lab adjudicated rhythm data for the primary effectiveness endpoint, and an independent Clinical Events Committee (CEC) adjudicated primary

safety endpoint events. Additionally, an independent Data Safety Monitoring Board (DSMB) reviewed all safety data throughout the course of the study.

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the DIAMOND-AF Study was limited to patients who met the following inclusion criteria:

   1) Above eighteen (18) years of age or of legal age to give informed consent specific to state and national law.
   2) Subjects with a history of symptomatic, PAF who have had ≥ 2 episodes of PAF reported within the 6 months prior to index ablation procedure with a physician note indicating recurrent, self-terminating AF.
   3) At least one episode of PAF documented by electrocardiographic data within 12 months prior to index ablation procedure.
   4) Refractory to at least one Class I-IV anti-arrhythmic AAD for treatment of PAF.
   5) Suitable candidate for intra-cardiac mapping and ablation of arrhythmia.
   6) Subject agrees to comply with study procedures and be available (geographically stable) for follow-up visits for at least 12 months after enrollment.
   7) Subject is willing and able to provide written consent.

   Patients were not permitted to enroll in the DIAMOND-AF Study if they met any of the following exclusion criteria:

   At time of enrollment and/or prior to procedure:
   1) AF secondary to electrolyte imbalance, thyroid disease or reversible or noncardiac cause.
   2) LA diameter > 5.5 cm.
   3) Left ventricular ejection fraction (LVEF) < 35%.
   4) Currently New York Heart Association (NYHA) Class III or IV or exhibits uncontrolled heart failure.
   5) Body Mass Index (BMI) > 40 kg/m^2.
   6) LA ablation, septal closure device or mitral valve surgical procedure at any time prior to enrollment.
   7) Presence of intramural thrombus, tumor or abnormality that precludes vascular access, catheter introduction or manipulation.
   8) Coagulopathy, bleeding diathesis or suspected procoagulant state.

9) Sepsis, active systemic infection or fever (>100.5°F / 38°C) within a week prior to the ablation procedure.

10) Significant restrictive or obstructive pulmonary disease or chronic respiratory condition.

11) Renal failure requiring dialysis or renal compromise that in the investigator's judgement would increase risk to the subject or deem the subject inappropriate to participate in the study.

12) Known allergies or intolerance to anticoagulant and antiplatelet therapies to be used in conjunction with the study or contrast sensitivity that cannot be adequately pre-treated prior to the ablation procedure.

13) Positive pregnancy test results for female subjects of childbearing potential or breast feeding.

14) Enrollment in a concurrent clinical study that in the judgement of the investigator would impact study outcomes.

15) Acute or chronic medical condition that in the judgment of the investigator would increase risk to the subject or deem the subject inappropriate to participate in the study.

16) Life expectancy < 12 months based on medical history or the medical judgement of the investigator.

Within 1 month of enrollment or just prior to procedure:

17) Documented LA thrombus upon imaging.

18) Creatinine >2.5mg/dl or creatinine clearance <30mL/min.

Within 2 months of enrollment:

19) Regularly (uninterrupted) prescribed amiodarone.

Within 3 months of enrollment:

20) Significant gastrointestinal (GI) bleed.

21) Myocardial infarction (MI), unstable angina, cardiac surgery or coronary intervention.

Within 6 months of enrollment:

22) Coronary artery bypass graft (CABG) procedure.

23) Implantable Cardioverter Defibrillation (ICD), Cardiac Resynchronization Therapy (CRT) leads or pacemaker implant procedure.

24) Documented stroke, Cerebrovascular Accident (CVA), Transient Ischemic Attack (TIA) or suspected neurological event.

Within 12 months of enrollment:

25) An episode of AF lasting >7 days in duration.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at baseline, operative/discharge, 7 days, 1, 3, 6, and 12 months following the index procedure. All patients were followed per protocol in relation to the date of the index ablation procedure. Clinical data were required to be collected at all subject visit intervals. Adverse events and complications were recorded at all visits. Post-ablation rhythm monitoring included symptomatic and twice monthly symptomatic/asymptomatic event monitor transmissions during the evaluation period, ECG at 3, 6, and 12 months, and 24-hour Holter monitor at 6 and 12 months.

The key timepoints are shown below in **Table 9** summarizing schedule of treatments and evaluations.

Table 9. Schedule of Treatments and Evaluations

Assessments/ Activities	Baseline Evaluation	Ablation Procedure	Blanking Period (Ablation Procedure – 3 Months Post Procedure)				Effectiveness Evaluation Period (3 Months -12 Months Post Procedure)		
			Pre-Discharge	7-Day (± 3 days)	1-M (± 14 days)	Repeat Ablation	3-M (± 21 days)	6-M (± 28 days)	12-M (± 45 days)
Eligibility Screening	X								
Informed Consent	X								
Subject Demographics	X								
Medical History	X								
Physical Exam	X		X		X	X[A]	X	X	X
12-lead ECG		X	X		X	X[A]	X	X	X
TEE or TTE	X[B]								
TEE or ICE[G]		X[C]				X[C]			
Chest CT / MRI							X[F]	X[F]	X[F]
NIH Stroke Scale	X		X			X[A]			X
Procedural Data		X				X[A]			
Event Monitor Recording			X[D]	X[D]	X[D]		X[E]	X[E]	X[E]
24 hr. Holter Monitor								X	X
Cardiac Medication Changes	X	X	X	X	X	X[A]	X	X	X
Protocol Deviations	X	X	X	X	X	X[A]	X	X	X
Adverse Events	X	X	X	X	X	X[A]	X	X	X
AF Quality of Life Survey (AFEQT)	X					X[A]		X	X

[A] Only required if a repeat ablation procedure performed. 1 repeat ablation procedure was allowed during Blanking Period.

[B] TEE or TTE only required if subject does not have imaging data to determine LA diameter, LVEF for eligibility within 180d of ablation procedure

[C] TEE or ICE required pre-procedure to rule out LA thrombus if any of the following were met: CHA2DS2-VASc score was ≥ 2, if LA diameter ≥4.6 or if pre-procedure anticoagulation requirements were not met

[D] Event monitor recording only required if subject was experiencing symptoms during blanking period

[E] Following the blanking period (3-12 month following ablation), subjects were required to take two 1-minute event monitor recordings per month regardless of whether they were experiencing symptoms.

[F] Only required if subject presents with symptoms associated with PV stenosis

3. Clinical Endpoints

Primary Endpoints

The primary safety endpoint was defined as freedom from composite of serious adverse events (SAE) occurring within 30-days and clinically symptomatic pulmonary vein stenosis through 6-months post-index ablation procedure, as adjudicated by an independent Clinical Events Committee (CEC) for relatedness to the procedure or device.

The primary safety device- or procedure-related SAE composite was a combined rate of the following events:

- Atrioesophageal fistula
- Bleeding complication
- Cardiac tamponade / perforation
- Death
- Extended hospitalization*
- Myocardial infarction
- Pericarditis
- Phrenic nerve paralysis
- Pulmonary edema
- Pulmonary vein stenosis
- Stroke post-ablation
- Thromboembolism
- Transient ischemic attack (TIA) post-ablation
- Vagal nerve injury
- Vascular access complications

* Extended hospitalization is defined as extended hospital stay or re-hospitalization that is related to the procedure or device.

The primary effectiveness endpoint was defined as freedom from documented AF, AFL* and AT episodes following the blanking period (3-month follow-up post-ablation procedure) through the end of the effectiveness evaluation period (12-month follow-up post-ablation procedure).

An effectiveness failure was defined by any of the following events:

- Inability to electrically isolate all accessible targeted pulmonary veins during the ablation procedure**
- Documented episodes of AF, AFL or AT lasting ≥30 seconds in duration as evidenced by electrocardiographic data during the effectiveness evaluation period
- DC cardioversion for AF, AFL or AT during the effectiveness evaluation period
- A repeat ablation procedure to treat AF, AFL or AT during the effectiveness evaluation period
- Use of a new or modification to existing Class I-IV AAD regimen to treat AF, AFL or AT recurrence during the effectiveness evaluation period
- Use of a non-study device for ablation of any AF targets during the index or repeat ablation procedure during the blanking period
- More than one (1) repeat ablation procedure during the blanking period

** Occurrence and/or ablation of cavotricuspid isthmus (CTI)-dependent AFL, as confirmed by entrainment maneuvers during EP testing at any time during this study was not a primary effectiveness failure because it was not considered an iatrogenic arrhythmia following a left atrial ablation procedure for AF.*
***Electrical isolation as confirmed by demonstration of exit and/or entrance conduction block.*

The Primary Effectiveness and Primary Safety Endpoint analyses were performed on the Intention-to-Treat (ITT) Cohort to demonstrate non-inferiority of the investigational group (INV) to the control group (CTRL). The ITT cohort was comprised of all randomized subjects regardless of whether they received study treatment, with the following analyses conducted according to the randomized treatment assignment.

Primary Effectiveness Analysis:
The following primary effectiveness hypothesis was evaluated using the exact test for a binomial proportion at a one-sided significance level of 2.5%.

- $H_0: \pi_{INV} \leq \pi_{CTRL} - \delta$
- $H_1: \pi_{INV} > \pi_{CTRL} - \delta$

where π was the population proportion for the corresponding treatment group and δ was the non-inferiority margin of 12.5%.

Primary Safety Analysis
The following primary safety hypothesis was evaluated using the exact test for a binomial proportion at a one-sided significance level of 2.5%.

- $H_0: \pi_{INV} \leq \pi_{CTRL} - \delta$
- $H_1: \pi_{INV} > \pi_{CTRL} - \delta$

where π was the population proportion for the corresponding treatment group and δ was the non-inferiority margin of 6.5%.

Secondary Endpoints
Secondary endpoints to characterize the performance of the DiamondTemp Ablation System, relative to the control device, include:

1. Mean duration of individual RF ablations (seconds).
2. Mean cumulative RF time per procedure (minutes).
3. Freedom from a composite of SAE occurring within 7-days post-index ablation procedure as adjudicated by an independent CEC for relatedness to the procedure or device.

4. Freedom from documented AF, AT and AFL episodes following the blanking period through 12-month follow-up post-ablation procedure in the absence of class I and III anti-arrhythmic drug therapy.
5. Rate of acute procedural success, defined as confirmation of electrical isolation of PVs via assessment of entrance block at least 20 minutes following the last ablation around the respective PV.
6. Rate of single procedure success defined as the rate of subjects treated with one single ablation procedure during study participation and with freedom from documented AF, AT and AFL at 12 months.
7. Rate of single procedure success defined as the rate of subjects treated with one single ablation procedure during study participation and with freedom from ALL primary effectiveness endpoint failure criteria.
8. Rate of occurrence of electrically reconnected PVs following a 20-minute waiting period assessed by entrance block at index procedure.
9. Accumulated changes in Quality of Life (QOL) using the AF QOL Survey (AFEQT Questionnaire) from baseline through 6 and 12 months following ablation procedure.
10. Neurological changes measured using the NIH stroke scale between baseline and post-ablation (pre-discharge visit) and at 12 months post-ablation procedure.
11. Total procedure time (minutes), defined as time of first assigned ablation catheter insertion into the vasculature to time of last procedural ablation catheter removed.
12. Time to achieve initial PVI at index procedure (minutes), defined as time of delivery of first RF ablation with the assigned ablation catheter until confirmation of PVI.
13. Total treatment device time (minutes), defined as time of delivery of first RF ablation with the assigned ablation treatment catheter to removal of the treatment catheter.
14. Total number of RF ablations per procedure.
15. Total fluid infused through the assigned ablation catheter (mL).
16. Total fluoroscopy time (minutes).
17. Number of re-hospitalizations due to atrial fibrillation recurrence after blanking period.

Of the seventeen (17) pre-defined secondary endpoints above, four (4) specific secondary endpoints were evaluated for superiority over Control. The analytical

approach was one of *a priori* hierarchical hypotheses, with the pre-specified order of the endpoints as follows:

1. Mean duration of individual RF ablations (seconds).
2. Mean cumulative RF time per procedure (minutes).
3. Total fluoroscopy time (minutes).
4. Total procedure time (minutes), defined as time of first assigned ablation catheter insertion into the vasculature to time of last procedural ablation catheter removed.

The first secondary endpoint (i.e., RF ablation time) needs to be significant at the two-tailed α-level of 0.05, before the next one can be considered at the same threshold. Once an endpoint was determined to be non-significant, testing was to stop and any remaining hypotheses were not tested.

B. Accountability of PMA Cohort

At the time of database lock, of 485 patients consented in the PMA study, 455 (93.8%) patients were available for analysis at the completion of the study, the 12-month post-operative visit. A total of 482 subjects were enrolled and randomized (DiamondTemp: 239, Control: 243) in the DIAMOND-AF Study at 23 US and OUS centers. Of these, 14 DiamondTemp and 13 Control subjects exited the study before completing the study. The last subject exited the study on 12/3/2019. **Table 10** shows subject disposition. **Table 11** shows an accounting of follow-up visit attendance during the study. Subject accountability is further summarized in **Figure 5** below. The database was locked on 3/27/2020.

Table 10. Subject Disposition

Subject Disposition	**Number (N)**
Number of Subjects with Signed Consent	485
Number of Subjects Not Randomized	3
Documented Stroke, CVA, TIA or Suspected Neurological Event [1]	1
Enrollment Cap Met [2]	1
Regularly Prescribed Amiodarone [3]	1
Number of Subjects Enrolled/Randomized (Intention-to-Treat Analysis Cohort)	482

[1] Subject 15-021 met exclusion criterion #24

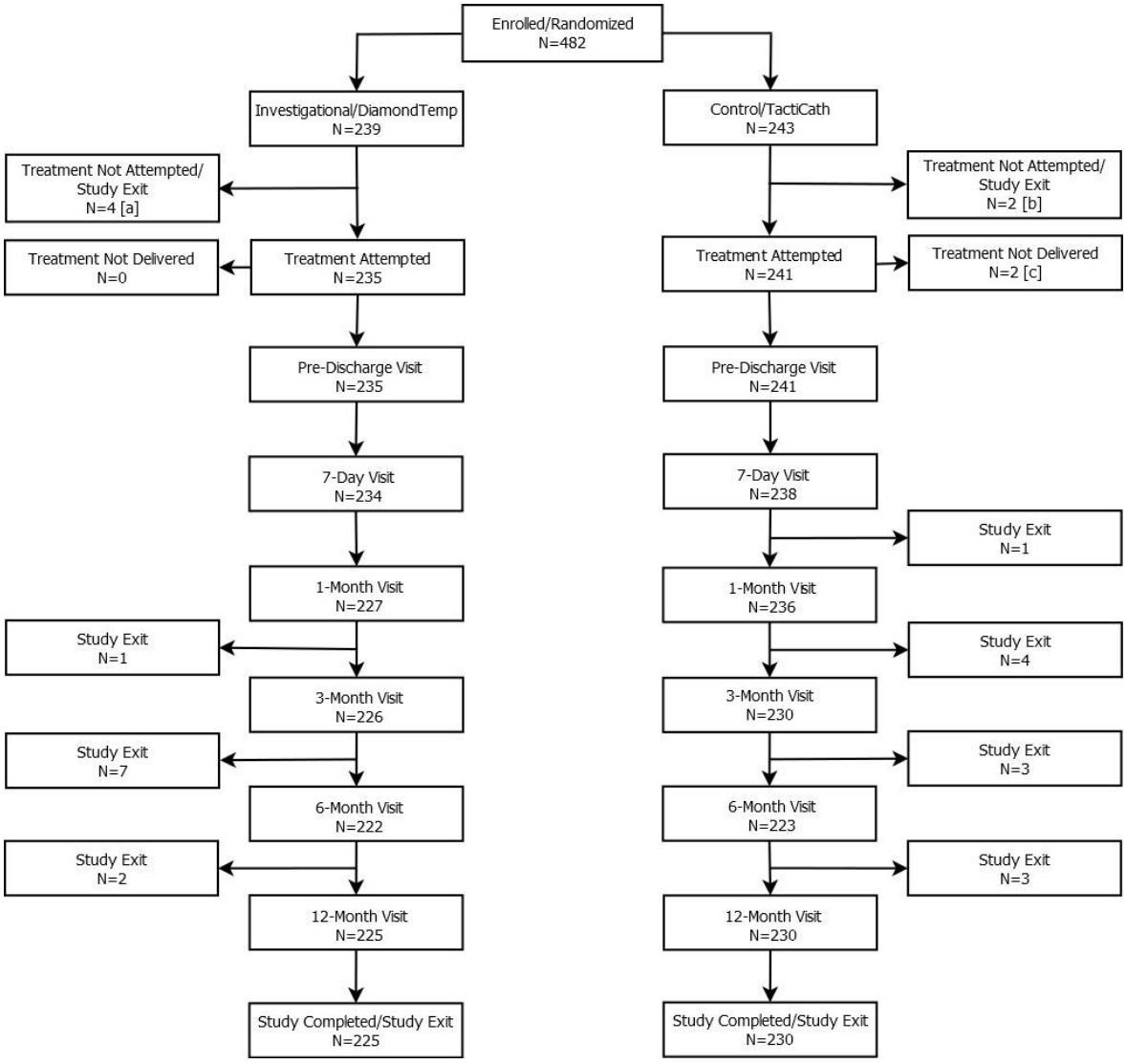
[2] Subject 15-010 met all criteria but was never randomized prior to study exit (30-Oct-2018), with a reason of "Subject's ablation was not scheduled and patient was not randomized prior to enrollment number being met"

[3] Subject 17-001 met exclusion criterion #19

Table 11. Scheduled Visit Compliance

Visit	Control (N=243)	DiamondTemp (N=239)	All Subjects (N=482)
Enrolled/Randomized	243 (100%)	239 (100%)	482 (100%)
Ablation Procedure	241 (99.2%)	235 (98.3%)	476 (98.8%)
Pre-Discharge Visit	241 (99.2%)	235 (98.3%)	476 (98.8%)
7 Day Visit	238 (97.9%)	234 (97.9%)	472 (97.9%)
1 Month Visit	236 (97.1%)	227 (95.0%)	463 (96.1%)
3 Month Visit	230 (94.7%)	226 (94.6%)	456 (94.6%)
6 Month Visit	223 (91.8%)	222 (92.9%)	445 (92.3%)
12 Month Visit	230 (94.7%)	225 (94.1%)	455 (94.4%)
Study Completion			
Completion of Study as Planned	230 (94.7%)	225 (94.1%)	455 (94.4%)
Discontinued Prematurely	13 (5.3%)	14 (5.9%)	27 (5.6%)

Figure 5. Subject Accountability FlowChart



[a] Subject withdrew consent (06-013); Subject progressed to persistent AF (11-001); Enrollment closure (09-003, 13-015).
[b] Enrollment closure (10-004); Physician no longer believed the subject was a good candidate for the study (11-004).
[c] Treatment attempted but not delivered with TactiCath due to technical difficulties (09-001); Treatment attempted but not delivered with TactiCath due to procedure failure (22-005).

Follow-up visit compliance was 91.8% or higher for all follow-up visits, with 94.7% of control subjects and 94.1% of DiamondTemp subjects completing the study as planned through the 12 month follow-up visit.

The protocol specified analysis populations include:

- *Intention-to-Treat (ITT)*: The 482 randomized subjects comprise the ITTpopulation.
- *Safety Analysis:* The 476 subjects who had a study ablation catheter inserted comprise the Safety Analysis cohort.
- *Per Protocol (PP)*: The PP population consisted of 451 subjects who met all eligibility criteria, had no major protocol deviations, and were treated in accordance with the randomization treatment assignment.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a paroxysmal atrial fibrillation catheter ablation study performed in the US. Tables 12, 13 and 15 summarize the demographics, baseline characteristics, and medical history for subjects by treatment group in the ITT cohort. Demographic data and baseline characteristics were balanced with no significant differences between the treatment groups except for history of non-AF/AFL arrhythmias or conduction disturbance.

Table 12 Demographic Characteristics, Intention-to-Treat Cohort, Control vs DiamondTemp

Demographics	**Control (N=243)**	**DiamondTemp (N=239)**
Age, years		
Mean (SEM / SD)	63.0 (0.67 / 10.42)	62.3 (0.72 / 11.13)
Median	64.0	65.0
Min, Max	27.0, 84.0	22.0, 82.0
N (N Missing)	243 (0)	239 (0)
Sex, n (%)		
Male	143 (58.8%)	136 (56.9%)
Female	100 (41.2%)	103 (43.1%)
Race, n (%)		
American Indian or Alaska Native	2 (0.8%)	3 (1.3%)
Asian	2 (0.8%)	0 (0%)
Black or African American	4 (1.6%)	4 (1.7%)
Other, specify: Caribbean	0 (0%)	1 (0.4%)
Other, specify: Ecuadorian	0 (0%)	1 (0.4%)
Prefer Not to Say	68 (28.0%)	66 (27.6%)
Unknown	6 (2.5%)	5 (2.1%)

White	161 (66.3%)	159 (66.5%)
Ethnicity, n (%)		
Hispanic or Latino	5 (2.1%)	6 (2.5%)
Not Hispanic or Latino	169 (69.5%)	167 (69.9%)
Prefer Not to Say	69 (28.4%)	66 (27.6%)

Min = Minimum, Max = Maximum; SD= Standard Deviation; SEM=Standard Error of the Mean.
Notes: N = Number of subjects in the population. n = Number of subjects in the specific category. Percentages are calculated as 100 x (n/N).
Age is derived from the date of informed consent.

Table 13. Baseline Characteristics, Intention-to-Treat Cohort, Control vs DiamondTemp

Baseline Characteristics	**Control (N=243)**	**DiamondTemp (N=239)**	**p-value**
Height, cm			0.7480
Mean (SEM / SD)	172.7 (0.63 / 9.89)	172.9 (0.63 / 9.69)	
Median	172.7	172.7	
Min, Max	152.0, 196.0	147.3, 205.7	
N (N Missing)	243 (0)	239 (0)	
Weight, kg			0.2821
Mean (SEM / SD)	85.4 (1.03 / 16.01)	84.1 (1.17 / 18.06)	
Median	85.0	83.0	
Min, Max	51.0, 146.0	45.8, 131.7	
N (N Missing)	243 (0)	239 (0)	
BMI, kg/m2			0.2422
Mean (SEM / SD)	28.6 (0.29 / 4.48)	28.0 (0.32 / 5.00)	
Median	28.1	27.5	
Min, Max	19.8, 42.9	14.2, 44.1	
N (N Missing)	243 (0)	239 (0)	
Serum Creatinine, mg/dL			0.9254
Mean (SEM / SD)	0.9 (0.01 / 0.22)	0.9 (0.02 / 0.23)	
Median	0.9	0.9	
Min, Max	0.1, 1.6	0.5, 2.2	
N (N Missing)	227 (16)	223 (16)	
LVEF, %			0.4905
Mean (SEM / SD)	60.1 (0.45 / 7.08)	59.8 (0.47 / 7.19)	
Median	60.0	60.0	
Min, Max	38.0, 80.0	44.0, 82.0	
N (N Missing)	243 (0)	235 (4)	
LA Diameter, cm			0.5014

Mean (SEM / SD)	4.1 (0.04 / 0.67)	4.0 (0.04 / 0.59)	
Median	4.0	4.0	
Min, Max	2.2, 5.5	2.5, 5.5	
N (N Missing)	243 (0)	233 (6)	
NYHA Functional Class, n (%)			0.9581
Class I	36 (14.8%)	32 (13.4%)	
Class II	20 (8.2%)	22 (9.2%)	
Class III	0 (0%)	0 (0%)	
Class IV	0 (0%)	0 (0%)	
NA (1)	117 (48.1%)	116 (48.5%)	
Unknown (2)	70 (28.8%)	69 (28.9%)	
Heart Rate, bpm			0.7079
Mean (SEM / SD)	69.3 (1.23 / 19.23)	69.0 (1.12 / 17.37)	
Median	64.0	65.0	
Min, Max	36.0, 169.0	35.0, 140.0	
N (N Missing)	243 (0)	239 (0)	
Systolic BP, mmHg			0.2999
Mean (SEM / SD)	136.3 (1.25 / 19.41)	138.1 (1.28 / 19.82)	
Median	133.0	135.0	
Min, Max	92.0, 206.0	77.0, 199.0	
N (N Missing)	243 (0)	239 (0)	
Diastolic BP, mmHg			0.9374
Mean (SEM / SD)	77.4 (0.70 / 10.94)	77.5 (0.69 / 10.73)	
Median	78.0	78.0	
Min, Max	46.0, 110.0	43.0, 104.0	
N (N Missing)	243 (0)	239 (0)	
CHA_2DS_2-VASc Score			0.2410
Mean (SEM / SD)	2.11 (0.10 / 1.50)	1.92 (0.09 / 1.38)	
Median	2.0	2.0	
Min, Max	0.0, 7.0	0.0, 6.0	
N (N Missing)	243 (0)	239 (0)	

BMI=Body Mass Index; BP=Blood Pressure; LA=Left Atrium; LVEF=Left Ventricular Ejection Fraction; NYHA=New York Heart Association.
Min = Minimum, Max = Maximum; SD = Standard Deviation; SEM=Standard Error of the Mean.
(1) Subjects without heart failure, will have an NYHA result that is not applicable (NA).

(2) NYHA score is missing/not available in source documents.

Table 14 shows years since first diagnosis of atrial fibrillation and history of AAD therapy for subjects by treatment group in the Intention-to-Treat cohort.

Table 14. History of Atrial Fibrillation and ADD Therapy, Intent-to-Treat Cohort, Control vs DiamondTemp

Medical History	Control (N=243)	DiamondTemp (N=239)
Years Since First Diagnosis (years)		
Mean (SEM / SD)	4.0 (0.34 / 4.85)	3.5 (0.33 / 4.68)
Median	2	2
Min, Max	0, 26	0, 28
N (N Missing)	205 (38)	207 (32)
AAD Use History		
Subjects with History of AAD Use and Failed/Not Tolerate, n(%)	243 (100.0%)	239 (100.0%)
Subjects with History of Class I/III AAD Use and Failed/Not Tolerate, (*), n(%)	191 (78.6%)	187 (78.2%)
Subjects with History of Class II/IV AAD Use and Failed/Not Tolerate, (*), n(%)	121 (49.8%)	117 (49.0%)

AAD=Anti-arrhythmic drugs; AF=Atrial Fibrillation; PAF=Paroxysmal Atrial Fibrillation
Min = Minimum, Max = Maximum; SD=Standard Deviation; SEM=Standard Error of the Mean.
Notes: N = Number of subjects in the population. n = Number of subjects in the specific category. Percentages are calculated as 100 x (n/N).
All other percentages are calculated as 100 x (n/N1). N1 = Number of subjects in category.
(*) Categories are not mutually exclusive and subjects may count in more than one category.

Table 15. Medical History, Intention-to-Treat Cohort, Control vs DiamondTemp

Medical History	Control (N=243)	DiamondTemp (N=239)
Atrial Flutter	51 (21.0%)	46 (19.2%)
Hypertension Requiring Medication	137 (56.4%)	124 (51.9%)
Hypertension Regardless of Medications Required	138 (56.8%)	125 (52.3%)
Diabetes	28 (11.5%)	20 (8.4%)
Structural Heart Disease	7 (2.9%)	7 (2.9%)
Cerebrovascular Accident/Transient Ischemic Attack	20 (8.2%)	12 (5.0%)
Thromboembolic Events	6 (2.5%)	4 (1.7%)
Coronary Artery Disease	29 (11.9%)	27 (11.3%)
Myocardial Infarction	2 (0.8%)	4 (1.7%)
Non-PAF/AFL Arrhythmias or conduction disturbance	42 (17.3%)	22 (9.2%)
Vascular Disease	20 (8.2%)	13 (5.4%)
Congestive Heart Failure	3 (1.2%)	6 (2.5%)

Previous CABG Procedure	1 (0.4%)	0 (0%)
Previous ICD/CRT/Pacemaker Implant	0 (0%)	1 (0.4%)
Gastrointestinal (GI) Disease	25 (10.3%)	28 (11.7%)
Pulmonary Disease with Different Etiologies	4 (1.6%)	6 (2.5%)
Sleep Apnea	45 (18.5%)	24 (10%)
Other	159 (65.4%)	149 (62.3%)
Smoking History - Yes	75 (30.9%)	71 (29.7%)
Smoking History – Current Smoker	16 (6.6%)	17 (7.1%)
Smoking History – Previously Smoked	59 (24.3%)	54 (22.6 %)
Class I or III AAD at Baseline	141 (58.0%)	125 (52.3%)

CABG=Coronary Artery Bypass Graft; CRT= Cardiac resynchronization therapy; ICD= implantable cardioverter defibrillator; PAF= Paroxysmal Atrial Fibrillation
Notes: N = Number of subjects in the population. n = Number of subjects in the specific category. Percentages are calculated as 100 x (n/N). Categories are not mutually exclusive and subjects may count in more than one category.

D. Procedure and Follow-up Data

1. Procedure Data

Table 16 presents the index ablation procedure characteristics by treatment group. Ablation time, fluoroscopy time and procedural duration were formally tested for superiority in the secondary analysis.

Table 16. Index Ablation Procedure Characteristics, Intention-to-Treat Control vs DiamondTemp

Procedural Characteristics	**Control (N=243)**	**DiamondTemp (N=239)**
Total Number of AF Index Ablation Procedures[N1]	241	235
TEE for LA Thrombus Screening Performed	236 (97.9%)	234 (99.6%)
Esophageal Monitoring/Protection:		
Esophageal Deviation, n (%)	22 (9.1%)	19 (8.1%)
Use of Esophageal Temperature Probe, n (%)	191 (79.3%)	186 (79.1%)
Ablation Parameter Settings – Max Power Set Point		
Mean (SEM/SD)	33.3 (0.39/6.01)	49.7 (0.24/3.74)
Median	30.0	50.0
Min, Max	5.0, 70.0	0.0, 56.0
N (N Missing)	239 (2)	233 (2)
Ablation Parameter Settings – Max Temperature Set Point		
Mean (SEM/SD)	44.1 (0.32/4.94)	59.9 (0.10/1.60)
Median	43.0	60.0

Min, Max	30.0, 70.0	43.0, 65.0
N (N Missing)	233 (8)	234 (1)
Non-PVI Ablation Targets(*):		
Type I CTI Flutter	69 (28.6%)	74 (31.5%)
Posterior Wall	3 (1.2%)	4 (1.7%)
Focal Triggers	2 (0.8%)	4 (1.7%)
Roof	2 (0.8%)	2 (0.9%)
SVC	3 (1.2%)	1 (0.4%)
CFAE	2 (0.8%)	1 (0.4%)
Flutter Line	2 (0.8%)	1 (0.4%)
Mitral Isthmus Line	2 (0.8%)	1 (0.4%)
AVRT/AVNRT	1 (0.4%)	1 (0.4%)
Incidence of Steam Pops, n (%)	5 (2.1%)	7 (3.0%)
Incidence of Char or Coagulum, n(%)	0 (0%)	0 (0%)

AF=Atrial Fibrillation; CTI=Cavotricuspid Isthmus; LA= Left Atrium; PV=Pulmonary Vein; TEE =Transesophageal echocardiography.Min = Minimum, Max = Maximum; SD=Standard Deviation; SEM=Standard Error of the Mean.Notes: N = Number of subjects in the Intention-to-Treat Population.n = Number of subjects in the specific category. Percentages are calculated as 100 x (n/N1). N1 = Number of subjects in category.(*) Categories are not mutually exclusive and subjects may count in more than one category.

2. Treatment During Blanking period

Table 17 presents the additional intervention performed to maintain sinus rhythm during the blanking period. Comparable number of subjects between the two arms received repeat ablation or cardioversion before the evaluation period.

Table 17. Additional Treatment During the Blanking Period

Subjects with Additional Treatment during Blanking Period	**Control (N=243)**	**DiamondTemp (N=239)**	**P-value***
Repeat ablation	11 (4.53%)	10 (4.18%)	1.00
Cardioversion	11 (4.53%)	7 (2.93%)	0.47
*P-value is calculated using two-sided Fisher's exact test			

3. Rhythm Monitoring Compliance

Post-ablation rhythm monitoring included symptomatic and twice monthly symptomatic/asymptomatic event monitor transmissions during the evaluation period, ECG at 3, 6, and 12 months, and 24-hour Holter monitor at 6 and 12 months. **Table 18** presents the rhythm monitoring compliance for each group. The two groups had similar adherence across different monitoring methods.

Table 18. Rhythm Monitoring Compliance

Rhythm Monitoring Method	Control (N=243)	DiamondTemp (N=239)	All Subjects (N=482)
12-Lead ECGs			
3 Month Visit 12-Lead ECG	219/237 (92.4%)	209/235 (88.9%)	428/472 (90.7%)
6 Month Visit 12-Lead ECG	206/234 (88.0%)	207/228 (90.8%)	413/462 (89.4%)
12 Month Visit 12-Lead ECG	224/231 (97.0%)	223/227 (98.2%)	447/458 (97.6%)
24-hour Holter Monitor			
6 Month Visit 24-hour Holter Monitor	202/234 (86.3%)	199/228 (87.3%)	401/462 (86.8%)
12 Month Visit 24-hour Holter Monitor	213/231 (92.2%)	204/227 (89.9%)	417/458 (91.0%)
TTMs			
(Total) Transmitted TTMs	5419	4557	9976
Expected TTMs	4373	4288	8661
Overall TTM Compliance (Subject) (%)			
Mean (SEM/SD)	60.5 (2.02/31.01)	61.3 (2.09/32.03)	60.9 (1.45/31.49)
Median	70.0	72.2	72.2
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0
N (N Missing)	236 (7)	235 (4)	471 (11)

ECG= Electrocardiogram;

Notes: N = Number of subjects in the Intention-to-Treat Population. n = Number of subjects in the specific category. For ECG and Holter, percentages for populations are calculated as 100 x (n/expected number of measurements at that visit).

Six subjects were randomized/enrolled but did not undergo index ablation procedure (06-013, 09-003, 10-004, 11-001, 11-004, 13-015).

TTM= Trans-telephonic Monitor.

Six subjects were randomized/enrolled but did not undergo index ablation procedure (06-013, 09-003, 10-004, 11-001, 11-004, 13-015).

[1] Subject Expected TTM is 2 if the subject's study participation in a given month is longer than 15 days, otherwise it is 1 for that month.

[2] Overall compliance is defined on a per subject basis and is based on a subject average monthly compliance rates over months 1 through 10 after the blanking period. A subject's monthly compliance rate is defined as minimum (TTM transmitted for that month, TTM expected for that month)/TTM expected for that month, over months 1 through 10 after the blanking period

E. Safety and Effectiveness Results

1. Safety Results

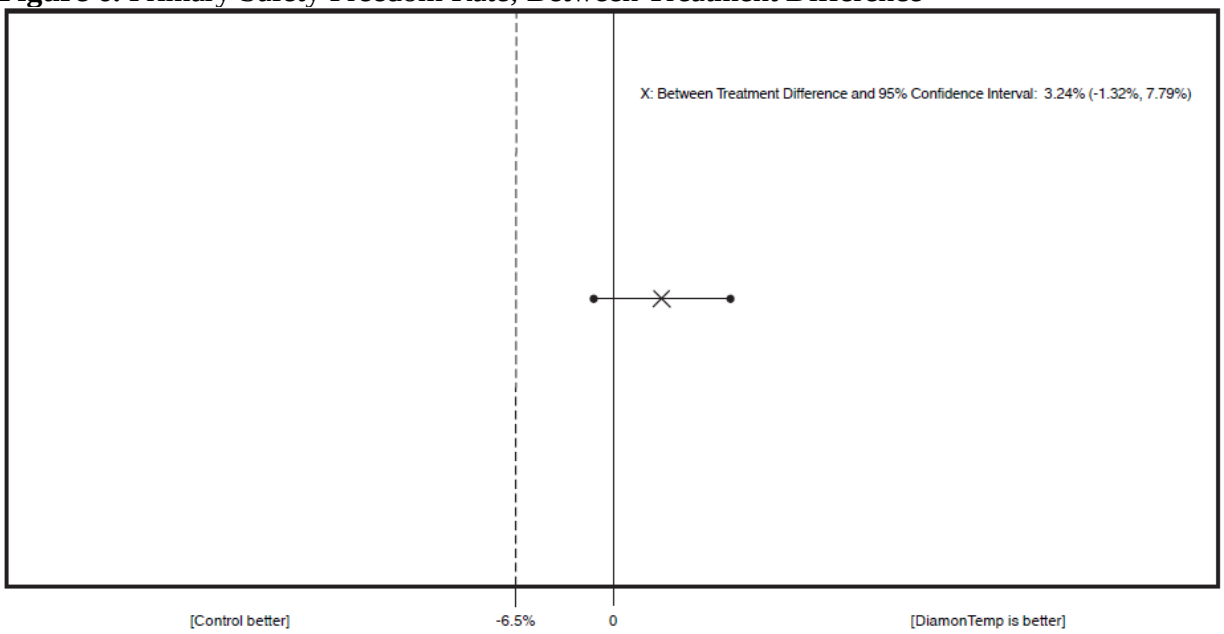
i. Primary Safety Endpoint

The primary safety analysis includes all randomized ITT subjects (243 Control and 239 DiamondTemp). There were 16 (6.6%) Control subjects and 8 (3.3%) DiamondTemp subjects that experienced at least one CEC-adjudicated primary safety endpoint event that contributed to the primary safety endpoint. The primary safety event freedom rate was 96.7% for the DiamondTemp group and 93.4% for the Control group. The difference (DiamondTemp – Control) in the primary safety endpoint freedom was 3.24% (95% CI: -1.32%, 7.79%), and the lower 97.5% confidence bound of -1.32% exceeded the pre-specified non-inferiority margin (NIM) of -6.5%. The primary safety endpoint was met ($p < 0.0001$, **Table 19**).

Table 19. Primary Safety Result, Intention-to-Treat Cohort

Primary Safety Endpoint: Freedom from Primary Safety Event as Adjudicated by the CEC	**Control (N=243) Number (%) (95% CI)**	**DiamondTemp (N=239) Number (%) (95% CI)**	**Difference (95% CI)**	**Farrington-Manning p-value (Non-inferiority Test)**
Total, By Subject	227 (93.4%) (89.5%, 96.2%)	231 (96.7%) (93.5%, 98.5%)	3.24% (-1.32%, 7.79%)	<0.0001

Figure 6. Primary Safety Freedom Rate; Between Treatment Difference



There were 24 Primary Safety Endpoint events reported in 24 subjects. **Table 20** summarizes the events that met the primary safety endpoint. Specifically, there were 16 subjects that met the primary safety endpoint in the control group and 8 subjects that met the primary safety endpoint in the DiamondTemp group. The most common primary safety endpoint met in the control group was extended hospitalization (6 subjects) followed by vascular access site complication (4 subjects). No more than 2 subjects met any of the individual primary safety endpoint events in the DiamondTemp group.

Table 20 CEC Adjudicated Primary Safety Endpoint Events (Intention-to-Treat Cohort)

CEC Adjudicated Adverse Events Contributing to the Primary Safety Endpoint	**Control By Subject (N_S=243) n (%)**	**DiamondTemp By Subject (N_S=239) n (%)**
Atrioesophageal Fistula	0 (0%)	0 (0%)
Bleeding Complication	0 (0%)	0 (0%)
Cardiac Tamponade/Perforation	2 (0.8%)	2 (0.8%)
Cardiovascular-Related Death Post-Ablation	0 (0%)	0 (0%)
Clinically Symptomatic Pulmonary Vein Stenosis at 6 Months Post-Index Ablation Procedure	0 (0%)	0 (0%)
Extended Hospitalization	6 (2.5%)*	0 (0%)
Myocardial Infarction	0 (0%)	0 (0%)
Pericarditis	1 (0.4%)	0 (0%)
Phrenic Nerve Paralysis	0 (0%)	1 (0.4%)
Pulmonary Edema	1 (0.4%)	0 (0%)

Stroke Post Ablation	1 (0.4%)	0 (0%)
Thromboembolism	0 (0%)	0 (0%)
Transient Ischemic Attack	1 (0.4%)	2 (0.8%)
Vagal Nerve Injury	0 (0%)	1 (0.4%)
Vascular Access Complication	4 (1.6%)	2 (0.8%)
Total	16 (6.6%)	8 (3.3%)

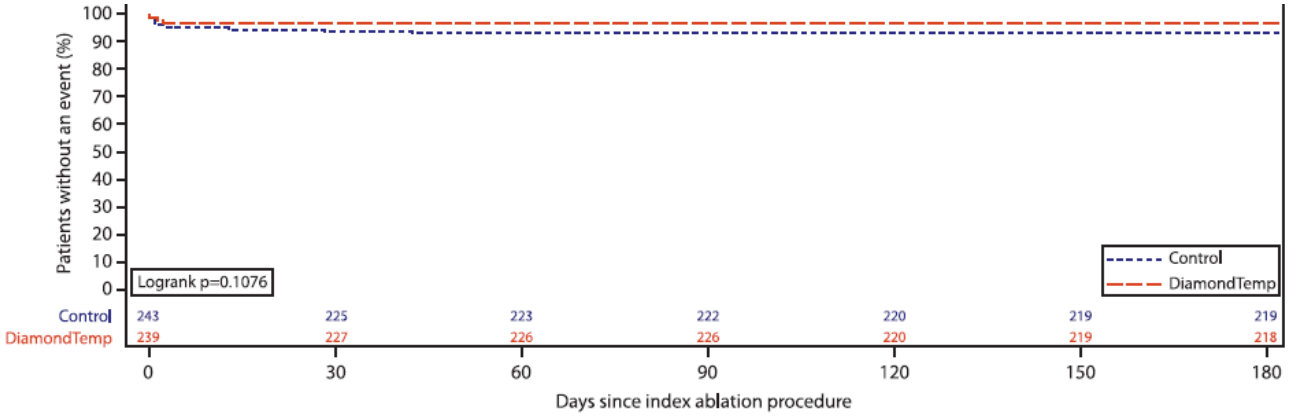
*Reasons for extended hospitalization include hematoma, pericardial effusion (< 1 cm), fever and chill, bladder outlet obstruction with UTI, hypotension, chest pain.
Notes: Ns = Number of subjects in the population. n = Number of subjects in the specific category.
Subject based percentages are calculated as 100 x (n/Ns).
Ne = Number of events in the Population. n2 = Number of events in the specific category.
Event based percentages are calculated as 100 x (n2/Ne).
For the 'by Subject' columns, subjects reporting a particular adverse event more than once are only counted once by the event category.
For the 'by Event' columns, all events are counted.

Table 20 and **Figure 6** display the primary safety objective results for the ITT cohort. The primary safety event freedom rate was 96.7% for the DiamondTemp group and 93.4% for the control group. The DiamondTemp minus control group primary safety endpoint freedom rate was 3.24% with a two-sided 95% confidence interval of -1.32% to 7.79%. Since the lower two-sided 95% confidence limit of -1.32% exceeded the non-inferiority margin of -6.5%, the primary safety objective was met ($p < 0.0001$).

A Kaplan-Meier analysis was also performed to evaluate the primary safety endpoint as a sensitivity analysis. The Kaplan-Meier method allows subjects to be included in the analysis up until the time they fail the primary safety endpoint or are censored due to premature study exit.

Figure 7 displays the Kaplan-Meier estimates for the freedom from primary safety event through 6 months (180 days) post-index ablation procedure; the entire time period for which subjects were at risk for a primary safety event. Based on the Kaplan-Meier methodology the freedom from primary safety event at 6 months was 97% for the DiamondTemp group and 93% for the control group. The log-rank test indicated that there was no difference in the freedom from primary safety event between groups ($p=0.11$).

Figure 7. Kaplan- Meier Survival: Time to Failure of the Primary Safety Endpoint, Intention-to-Treat Cohort



Kaplan-Meier Survival: Time to Failure of the Primary Safety Endpoint, Intention-to-Treat Cohort				
		Month 1	**Month 3**	**Month 6**
Control	Number at Risk	225	222	219
	Kaplan-Meier Estimate	0.9 4	0.9 3	0.9 3
	Standard Error	0.0155	0.0160	0.0160
DiamondTemp	Number at Risk	227	226	218
	Kaplan-Meier Estimate	0.9 7	0.9 7	0.9 7
	Standard Error	0.0117	0.0117	0.0117

Table 21 displays the primary safety endpoint status by treatment group and geography and indicates that the primary safety endpoint results were consistent by geography (Breslow-Day p-value = 0.54).

Table 21. Primary Safety Event Outcome: Relative Risk of Success; Overall and Stratified by Geographic Region and Treatment, Intention-to-Treat Cohort

Geographic Region	**Treatment**	**PSE Success**	**PSE Failure**	**Total**	**Relative Risk of Success**	**Breslow Day Test p-value**
Europe	DiamondTemp	124	5	129	1.02	0.5425
	Control	124	8	132		
North America	DiamondTemp	107	3	110	1.05	
	Control	103	8	111		
Overall	DiamondTemp	231	8	239	1.03	
	Control	227	16	243		
Pooled / Adjusted (CMH)[a]					1.03	

[a] CMH= Cochran-Mantel-Haenszel

The DIAMOND-AF Clinical Study met its primary safety objective (Intention-to-Treat Cohort). Primary safety endpoint success was observed in 227 (93.4%) control (TactiCath) subjects and 231 (96.7%) DiamondTemp subjects (95% CI for difference: -1.3% to 7.8%; p<0.0001 for non-inferiority). There was no evidence of heterogeneity in primary effectiveness outcome between treatment groups by geography (p=0.54). The DiamondTemp Ablation System demonstrated a reasonable assurance of safety for the treatment of drug refractory, recurrent, symptomatic PAF.

Summary of Adverse Events

Adverse events (AE) occurring during the study were continuously monitored and collected. There were no Unanticipated Adverse Device Effects or deaths reported in the DIAMOND-AF Clinical Study.

Table 22 summarizes all adverse events by seriousness and relatedness. In the ITT cohort, there were 171 adverse events reported in 98 (41.0%) of the 239 subjects randomized to the DiamondTemp group. Of these events, 21 events in 18 (7.5%) subjects were considered device or procedure related regardless of severity. There were 199 total adverse events reported in 103 (42.4%) of the 243 subjects randomized to the control group. Of these events, 35 events in 31 (12.8%) subjects were considered device or procedure related regardless of severity.

Table 22. AE Overall Summary Table, Intention-to-Treat Cohort, Control vs DiamondTemp

	Number of Events (Number of subjects, % of Subjects)	
Adverse Event Classification	**Control (N=243)**	**DiamondTemp (N=239)**
Total Adverse Events	199 (103, 42.4%)	171 (98, 41.0%)
Primary Safety Events[1]	16 (16, 6.6%)	8 (8, 3.3%)
Serious[2]		
Yes	61 (43, 17.7%)	53 (34, 14.2%)
No	138 (80, 32.9%)	118 (79, 33.1%)
Relatedness[2], [4]		
Device and/or Procedure Related[3]		
Related	35 (31, 12.8%)	21 (18, 7.5%)
Possibly Related	23 (18, 7.4%)	16 (15, 6.3%)
Unknown	2 (2, 0.8%)	0 (0, 0%)
Not Related	139 (79, 32.5%)	134 (81, 33.9%)
Device Relatedness		

Related	3 (3, 1.2%)	2 (2, 0.8%)
Possibly Related	4 (4, 1.6%)	3 (3, 1.3%)
Unknown	2 (2, 0.8%)	2 (2, 0.8%)
Not Related	190 (99, 40.7%)	164 (95, 39.7%)
Procedure Relatedness		
Related	35 (31, 12.8%)	21 (18, 7.5%)
Possibly Related	23 (18, 7.4%)	16 (15, 6.3%)
Unknown	2 (2, 0.8%)	0 (0, 0%)
Not Related	139 (79, 32.5%)	134 (81, 33.9%)

[1] Primary safety events are based on CEC adjudication.

[2] Seriousness and Relatedness are based on investigator assessment.

[3] Device and/or Procedure Relatedness- the strongest relationship with device or procedure is used in this category.

[4] A subject may count in more than one relatedness category.

All serious adverse events reported during this study are listed in **Table 23** by each treatment group.

Table 23 Serious Adverse Events by System Organ Class and Preferred Term, Intention-to-Treat Cohort

	Control		**DiamondTemp**	
System Organ Class Preferred Term	**By Event (N=61) n (%)**	**By Subject (N=243) n (%)**	**By Event (N=53) n (%)**	**By Subject (N=239) n (%)**
Total Subjects with at Least One SAE	NA	43 (17.7%)	NA	34 (14.2%)
Blood and Lymphatic System Disorders	3 (4.9%)	3 (1.2%)	1 (1.9%)	1 (0.4%)
Anemia	2 (3.3%)	2 (0.8%)	1 (1.9%)	1 (0.4%)
Blood Loss Anemia	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Cardiac Disorders	18 (29.5%)	17 (7.0%)	21 (39.6%)	17 (7.1%)
Arrhythmia Supraventricular	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Atrial Fibrillation	3 (4.9%)	3 (1.2%)	14 (26.4%)	10 (4.2%)
Atrial Flutter	6 (9.8%)	6 (2.5%)	2 (3.8%)	2 (0.8%)
Atrial Tachycardia	1 (1.6%)	1 (0.4%)	1 (1.9%)	1 (0.4%)
Atrioventricular Block Complete	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Cardiac Perforation	1 (1.6%)	1 (0.4%)	1 (1.9%)	1 (0.4%)
Cardiac Tamponade	1 (1.6%)	1 (0.4%)	1 (1.9%)	1 (0.4%)
Ischaemic Cardiomyopathy	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Pericardial Effusion	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Pericardial Haemorrhage	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Sinus Node Dysfunction	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)

Supraventricular Tachycardia	2 (3.3%)	2 (0.8%)	0 (0%)	0 (0%)
Gastrointestinal Disorders	4 (6.6%)	3 (1.2%)	2 (3.8%)	2 (0.8%)
Abdominal Pain	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Abdominal Pain Upper	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Dyspepsia	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Nausea	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Small Intestinal Obstruction	1 (1.6%)	1 (0.4%)	1 (1.9%)	1 (0.4%)
General Disorders and Administration Site Conditions	3 (4.9%)	3 (1.2%)	3 (5.7%)	3 (1.3%)
Chest Discomfort	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Chest Pain	2 (3.3%)	2 (0.8%)	2 (3.8%)	2 (0.8%)
Pyrexia	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Hepatobiliary Disorders	0 (0%)	0 (0%)	2 (3.8%)	2 (0.8%)
Cholelithiasis	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Hepatic Cirrhosis	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Immune System Disorders	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Allergy to Arthropod Sting	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Infections and Infestations	1 (1.6%)	1 (0.4%)	6 (11.3%)	5 (2.1%)
Appendicitis	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Colonic Abscess	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Diverticulitis	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Influenza	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Pneumonia	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Respiratory Tract Infection	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Wound Infection Staphylococcal	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Injury, Poisoning and Procedural Complications	8 (13.1%)	7 (2.9%)	4 (7.5%)	4 (1.7%)
Cranial Nerve Injury	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Foot Fracture	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Post Procedural Haematoma	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Vascular Access Complication	5 (8.2%)	5 (2.1%)	3 (5.7%)	3 (1.3%)
Venous Injury	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Metabolism and Nutrition Disorders	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Hemochromatosis	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Musculoskeletal and Connective Tissue Disorders	4 (6.6%)	3 (1.2%)	0 (0%)	0 (0%)
Arthritis	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Osteoarthritis	2 (3.3%)	1 (0.4%)	0 (0%)	0 (0%)
Spinal Osteoarthritis	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	1 (1.6%)	1 (0.4%)	1 (1.9%)	1 (0.4%)

Lung Adenocarcinoma	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Uterine Cancer	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Nervous System Disorders	6 (9.8%)	6 (2.5%)	7 (13.2%)	6 (2.5%)
Cerebrovascular Accident	1 (1.6%)	1 (0.4%)	1 (1.9%)	1 (0.4%)
Dizziness	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Dizziness Postural	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
IVth Nerve Paralysis	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Phrenic Nerve Paralysis	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Presyncope	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Sciatica	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Seizure Like Phenomena	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Transient Ischaemic Attack	1 (1.6%)	1 (0.4%)	3 (5.7%)	3 (1.3%)
Product Issues	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Device Pacing Issue	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Renal and Urinary Disorders	3 (4.9%)	3 (1.2%)	0 (0%)	0 (0%)
Renal Disorder	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Renal Failure	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Urinary Retention	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Reproductive System and Breast Disorders	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Prostatitis	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Respiratory, Thoracic and Mediastinal Disorders	3 (4.9%)	3 (1.2%)	2 (3.8%)	2 (0.8%)
Asthma	0 (0%)	0 (0%)	2 (3.8%)	2 (0.8%)
Haemoptysis	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Pneumothorax	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Pulmonary Oedema	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Surgical and Medical Procedures	2 (3.3%)	2 (0.8%)	3 (5.7%)	3 (1.3%)
Angioplasty	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Arthrodesis	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Colostomy	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Knee Arthroplasty	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)
Knee Operation	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Vascular Disorders	1 (1.6%)	1 (0.4%)	1 (1.9%)	1 (0.4%)
Hemorrhage	1 (1.6%)	1 (0.4%)	0 (0%)	0 (0%)
Hypertension	0 (0%)	0 (0%)	1 (1.9%)	1 (0.4%)

2. Effectiveness Results

i. Primary Effectiveness Endpoint

The primary effectiveness endpoint was defined as freedom from documented AF, AFL and AT episodes following the blanking period (3-month follow-up post-ablation procedure) through the end of the effectiveness evaluation period (12-month follow-up post-ablation procedure).

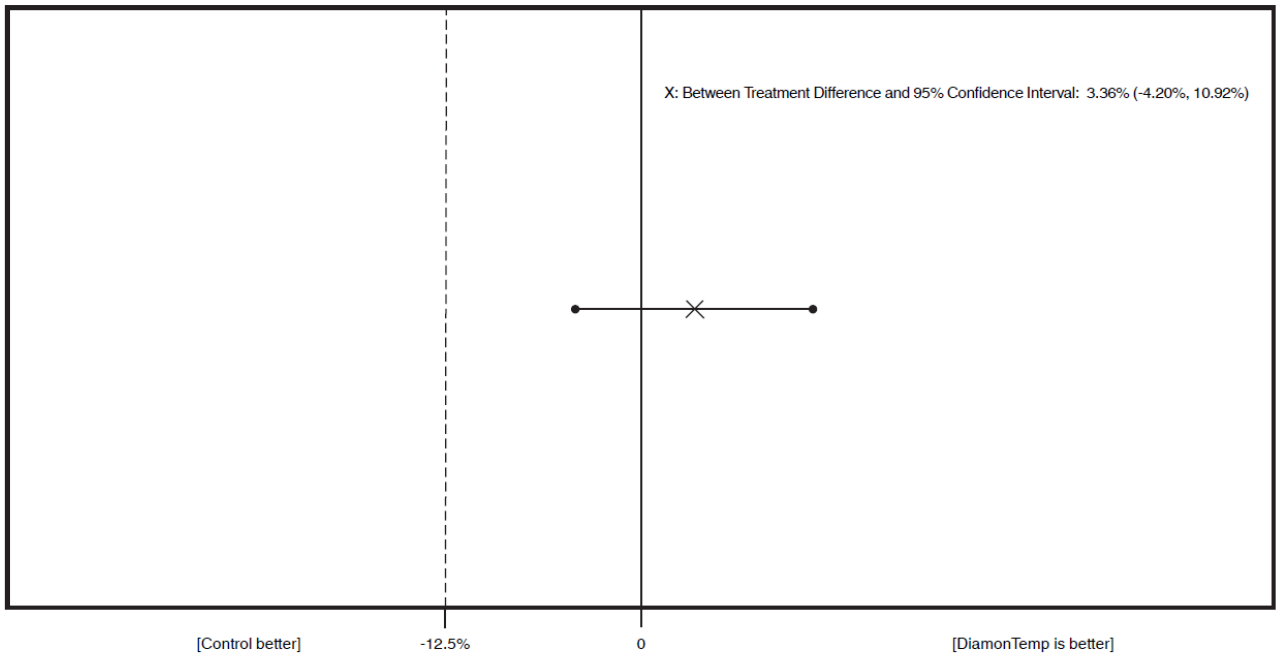
The analysis of effectiveness was based on the 482 subjects in the Intention-to-Treat cohort. Of the 243 randomized Control Subjects, 184 (75.7%) were free from all primary effectiveness endpoint failure criteria (**Table 24** and **Figure 8**). Of the 239 randomized DiamondTemp Subjects, 189 (79.1%) were free from all primary effectiveness endpoint failure criteria. The difference (DiamondTemp – Control) in freedom from primary effectiveness endpoint failure was 3.4%. The lower two-sided 95% confidence limit of -4.2% exceeded the non-inferiority margin of -12.5%, and the primary effectiveness endpoint was met (**Table 24**). The distribution of primary effectiveness failure modes was similar between the treatment group (**Table 25**).

Table 24. Primary Effectiveness Result, Intention-to-Treat Cohort

Primary Effectiveness Endpoint: Freedom from AF, AFL, AT During the Effectiveness Period	**Control (N=243) Number (%) (95% CI)**	**DiamondTemp (N=239) Number (%) (95% CI)**	**Difference (95% CI)**	**Farrington-Manning p-value (Non-inferiority Test)**
Total, By Subject[1],[2]	184 (75.7%) (69.8%, 81.0%)	189 (79.1%) (73.4%, 84.1%)	3.4% (-4.2%, 10.9%)	<0.0001

[1] In the total row, success is the absence of any of the criteria, while failure is the presence of one or more of the criteria.
[2] The Farrington-Manning Score test for non-inferiority (DiamondTemp minus Control) is used with a non-inferiority margin of -12.5%.

Figure 8. Primary Effectiveness: Between Treatment Difference



Confidence Intervals are based on Farrington and Manning's Likelihood Score Test

Table 25. Primary Effectiveness Failure Mode

	Control (N=243)		**DiamondTemp (N=239)**	
Criteria	**Success (No/Absent) n (%)**	**Failure (Yes/Present) n (%)**	**Success (No/Absent) n (%)**	**Failure (Yes/Present) n (%)**
Inability to electrically isolate all accessible targeted pulmonary veins during the ablation procedure.*	241 (99.2%)	2 (0.8%)	239 (100.0%)	0 (0%)
Documented episodes of AF, AFL or AT lasting ≥30 seconds in duration as evidenced by electrocardiographic data during the effectiveness evaluation period.	197 (81.1%)	46 (18.9%)	198 (82.8%)	41 (17.2%)
DC cardioversion for AF, AFL, or AT during the effectiveness evaluation period.	238 (97.9%)	5 (2.1%)	231 (96.7%)	8 (3.3%)
A repeat ablation procedure to treat AF, AFL or AT during the effectiveness evaluation period.	229 (94.2%)	14 (5.8%)	226 (94.6%)	13 (5.4%)

Use of a new or modification to existing Class I-IV anti-arrhythmic drug (AAD) regimen to treat AF, AFL or AT during the effectiveness evaluation period.	217 (89.3%)	26 (10.7%)	218 (91.2%)	21 (8.8%)
Use of a non-study device for ablation of any AF targets during the index or the repeat ablation procedure during the blanking period.	242 (99.6%)	1 (0.4%)	239 (100.0%)	0 (0%)
More than one (1) repeat ablation procedure during the blanking period.	243 (100.0%)	0 (0%)	239 (100.0%)	0 (0%)

*Either entrance and/or exit block
AAD=Anti-arrhythmic drugs; AF=Atrial Fibrillation; AFL=Atrial Flutter; AT=Atrial Tachycardia; DC=Direct Current.
Notes: N = Number of subjects in the Intent-to-Treat Population. n = Number of subjects in the specific category. Percentages are calculated as 100 x (n/N).
Subjects failing a particular criterion more than once are counted only once for that predefined category

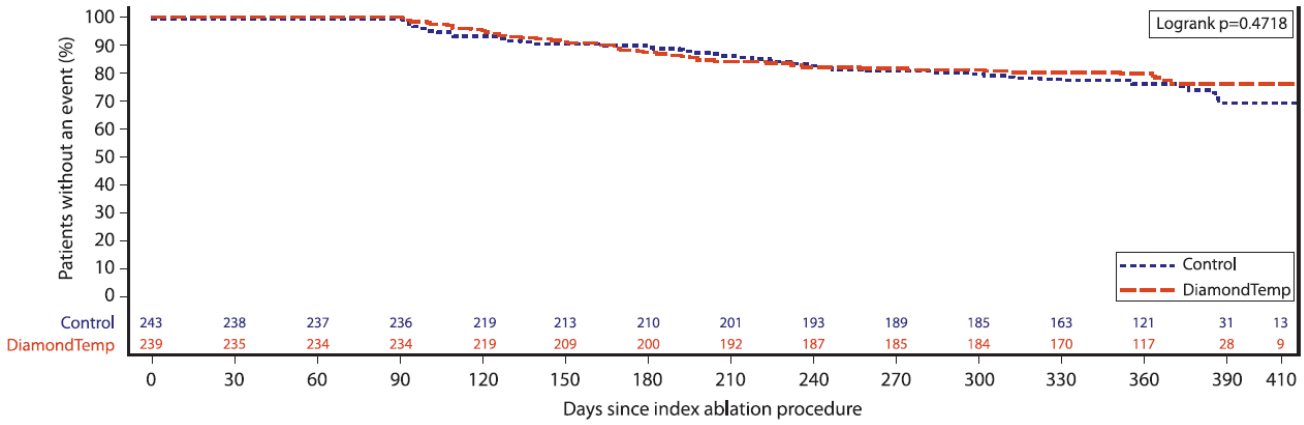
Sensitivity Analyses

Time-to-Event Analysis

A Kaplan-Meier analysis was also performed to evaluate the primary effectiveness endpoint as a sensitivity analysis. The Kaplan-Meier method allows subjects to be included in the analysis up until the time they fail the primary effectiveness endpoint or are censored due to premature study exit.

Figure 9 displays the Kaplan-Meier estimates for the freedom from primary effectiveness endpoint failure through 12 months post-ablation by treatment arm. Based on the Kaplan-Meier methodology the freedom from primary effectiveness endpoint failure at the end of the primary effectiveness period (day 410) post-ablation was 76% for the DiamondTemp group and 70% for the control group. The log-rank test suggested there was no difference in the freedom rate between groups (p=0.47).

Figure 9: Kaplan-Meier Survival: Time to Failure of the Primary Effectiveness Endpoint, Intention-to-Treat Cohort

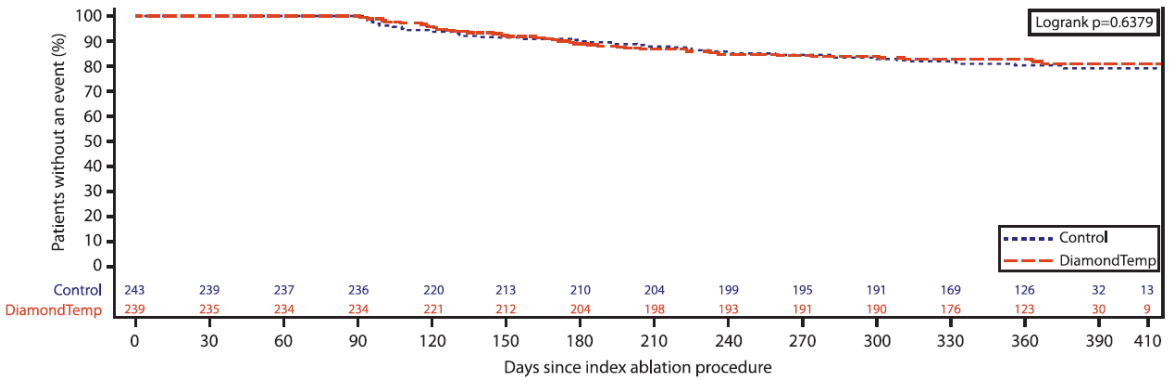


Kaplan-Meier Survival: Time to Failure of the Primary Effectiveness Endpoint, Intention-to-Treat Cohort					
		Month 3	Month 6	Month 9	Month 12
Control	Number at Risk	236	210	189	13
	Kaplan-Meier Estimate	0.99	0.89	0.81	0.70
	Standard Error	0.0058	0.0199	0.0256	0.0419
DiamondTemp	Number at Risk	234	200	185	9
	Kaplan-Meier Estimate	1.00	0.87	0.82	0.76
	Standard Error	0.0000	0.0219	0.0256	0.0309

3 Months (day 90), 6 Months (day 180), 9 Months (day 270), 12 Months (day 410)

An important component of the primary efficacy endpoint was the freedom from documented AF/AFL/AT episodes lasting 30 or more seconds following the 3-month blanking period through 12 months as identified on 24-hour Holter recordings, 12-lead ECG, or event monitor recordings (twice a month plus symptom driven). **Figure 10** displays Kaplan-Meier estimates for the freedom from documented AF/AFL/AT episodes lasting 30 or more seconds by treatment group. At 12 months post-ablation, Kaplan-Meier estimates for the freedom from documented AF/AFL/AT was 81% for the DiamondTemp group and 79% for the control group. The log-rank test indicated that there was no difference between treatment groups in the risk for AF/AFL/AT recurrence during the effectiveness evaluation period (p=0.64).

Figure 10. Kaplan-Meier Survival: Time to Documented AF/AFL/AT ≥ 30 Seconds, Intention-to-Treat Cohort



Kaplan-Meier Survival: Time to Documented AF/AFL/AT ≥ 30 Seconds, Intention-to-Treat Cohort					
		Month 3	Month 6	Month 9	Month 12
Control	# at Risk	236	210	195	13
	Kaplan-Meier Estimate	1.00	0.90	0.85	0.79
	Standard Error	0.0000	0.0194	0.0236	0.0290
DiamondTemp	# at Risk	234	204	191	9
	Kaplan-Meier Estimate	1.00	0.89	0.84	0.81
	Standard Error	0.0000	0.0205	0.0240	0.0270

3 Months (day 90), 6 Months (day 180), 9 Months (day 270), 12 Months (day 410)

Table 26 displays the primary effectiveness endpoint outcome by treatment group and geography. The Breslow-Day test indicated that there was no evidence for heterogeneity in primary effectiveness endpoint success rate between treatment groups by geography (p=0.36).

Table 26. Primary Effectiveness Endpoint: Relative Risk of Success; Overall and Stratified by Treatment and Geographic Region, Intention-to-Treat Cohort

Geographic Region	Treatment	PEE Success	PEE Failure	Total	Relative Risk of Success	Breslow Day Test p-value
Europe	DiamondTemp	93	36	129	1.01	0.3580
	Control	94	38	132		
North America	DiamondTemp	96	14	110	1.08	
	Control	90	21	111		
	DiamondTemp	189	50	239		

Overall	Control	184	59	243	1.04	
Pooled / Adjusted (CMH)[a]					1.04	

[a]CMH= Cochran–Mantel–Haenszel

The DIAMOND-AF Clinical Study met its primary effectiveness objective (Intention-to-Treat Cohort). Primary effectiveness endpoint success was observed in 184 (75.7%) control (TactiCath) subjects and 189 (79.1%) DiamondTemp subjects (95% CI for difference: -4.2% to 10.9%; p<0.0001 for non-inferiority). There was no evidence of heterogeneity in primary effectiveness outcome between treatment groups by geography (p=0.36). The DiamondTemp Ablation System demonstrated a reasonable assurance of effectiveness for the treatment of drug refractory, recurrent, symptomatic PAF.

Per Protocol Analysis

The per protocol analysis included 451 subjects who met all eligibility criteria, had no major protocol deviations, and treated in accordance with the randomization treatment assignment.

The primary effectiveness endpoint success was observed in 175 (of 229, 76.4%) Control subjects and 175 (of 222, 78.8%) DiamondTemp subjects.

Worst Case Scenario

Sensitivity analysis was performed using a worst case scenario in the safety cohort, in which all missing DiamondTemp data (n=8) were considered as primary effectiveness failures and all missing Control data (n=8) were considered as primary effectiveness successes. The difference of primary effectiveness success rate was -0.2% (95% CI: -8.0%, 7.6%), and the 97.5% lower confidence bound of -8.0% still met the predetermined NIM of -12.5% (**Table 27**)

Table 27. Primary Effectiveness Endpoint Sensitivity Analysis

Analysis	**Primary Effectiveness Endpoint Successes**		**95% CI for Difference**	**Farrington-Manning p-value (non-inferiority test)**
	Control (N=241)	**DiamondTemp (N=235)**		
Safety Cohort	182 (75.5%)	185 (78.7%)	(-4.4%, 10.8%)	<0.0001
Worst Case Scenario[1]	182 (75.5%)	177 (75.3%)	(-8.0%, 7.6%)	0.001

[1] The worst case scenario considered all Control subjects who had not failed the primary effectiveness endpoint at the time of their pre-mature exit as successes and all DiamondTemp subjects who had not failed the primary effectiveness endpoint prior to pre-mature exit as failures.

TTM compliance analysis

Table 28 presents the distribution of TTM compliance and the primary effectiveness success at each quartile between the two groups.

Table 28. TTM Monitoring Compliance and Primary Effectiveness Endpoint (PEE) Success per Quartile

PEE Status	**TTM Compliance**				
Frequency (Percentage)	**(0-25%]**	**(25-50%]**	**(50-75%]**	**(75-100%]**	**Total**
DiamondTemp					
Success	38 (84.44%)	23 (76.67%)	36 (65.45%)	88 (83.81%)	185
DiamondTemp N	45	30	55	105	235
Control					
Success	41 (82.00%)	28 (73.68%)	37 (68.52%)	76 (76.77%)	182
Control N	50	38	54	99	241

ii. Secondary Effectiveness Endpoints

A summary of DIAMOND-AF Study secondary effectiveness endpoint results are reported in **Table 29** below. The key secondary endpoints (1 – 4) were included in the prospectively specified hierarchical hypothesis testing with associated p-values.

Table 29. Secondary Endpoint Results, Intention-to-Treat Cohort, Control vs DiamondTemp

Secondary Endpoints, Intention-to-Treat Cohort, Control vs DiamondTemp			
Secondary Endpoints Results	**Control (N=243)**	**DiamondTemp (N=239)**	**p-value [1]**
Mean Duration of Individual RF Ablations (Seconds)			<0.0001
Mean (SEM / SD)	32.59 (1.642/25.34)	14.67 (0.343/5.260)	
95% CI	(29.4, 35.8)	(14.0, 15.4)	
Median	26.2	14.0	
Min, Max	8.9, 193.0	7.0, 47.4	
N (N Missing)	238 (5)	235 (4)	
Mean Cumulative RF Time Per Procedure (minutes)			<0.0001
Mean (SEM / SD)	29.80 (0.908/14.00)	17.93 (0.527/8.085)	
95% CI	(28.0, 31.6)	(16.9, 19.0)	

Median	25.9	16.0	
Min, Max	8.4, 83.2	2.5, 54.9	
N (N Missing)	238 (5)	235 (4)	
Total Fluoroscopy Time (minutes)			0.8528
Mean (SEM / SD)	12.83 (0.611/9.439)	12.66 (0.669/10.19)	
95% CI	(11.6, 14.0)	(11.3, 14.0)	
Median	10.58	9.95	
Min, Max	0.00, 60.05	0.00, 54.90	
N (N Missing)	239 (4)	232 (7)	
Total Procedure Time (minutes), Defined as Time of First Assigned Ablation Catheter Insertion Into the Vasculature to Time of Last Procedural Ablation Catheter Removed			
Mean (SEM / SD)	115.4 (3.28/50.84)	109.7 (3.01/46.18)	
95% CI	(108.9, 121.8)	(103.8, 115.6)	
Median	100.0	97.0	
Min, Max	37, 314	48, 389	
N (N Missing)	240 (3)	235 (4)	
Freedom from a composite of SAE occurring within 7-days post-index ablation procedure as adjudicated by an independent CEC for relatedness to the procedure or device.	230/243 (94.7%)	231/239 (96.7%)	
Freedom from documented AF, AT and AFL episodes following the blanking period through 12 month follow-up post-ablation procedure in the absence of class I and III anti-arrhythmic drug therapy	120/243 (49.4%)	142/239 (59.4%)	
Rate of acute procedural success, defined as confirmation of electrical isolation of PVs via assessment of entrance block at least 20 minutes following the last ablation around the respective PV	228/243 (93.8%)	228/239 (95.4%)	
Rate of single procedure success defined as the rate of subjects treated with one single ablation procedure during study participation and with freedom from documented AF, AT and AFL at 12 months	185/243 (76.1%)	183/239 (76.6%)	

Rate of single procedure success defined as the rate of subjects treated with one single ablation procedure during study participation and with freedom from ALL primary effectiveness endpoint failure criteria	173/243 (71.2%)	175/239 (73.2%)
Rate of occurrence of electrically reconnected PVs following a 20-minute waiting period assessed by entrance block at index procedure	45/243 (18.5%)	45/239 (18.8%)
Accumulated Changes in QoL Using the AF QoL Survey (AFEQT Questionnaire) from Baseline Through 6 and 12 Months Following Ablation Procedure		
At 6 Months:		
Mean (SEM / SD)	25.54 (1.569/22.68)	27.79 (1.606/23.10)
Median	22.2	25.0
Min, Max	-28.7, 86.1	-26.9, 98.1
N (N Missing)	209 (34)	207 (32)
At 12 Months:		
Mean (SEM / SD)	30.15 (1.570/23.23)	31.07 (1.599/23.44)
Median	26.9	26.9
Min, Max	-35.2, 86.1	-50.9, 98.1
N (N Missing)	219 (24)	215 (24)
Neurological Changes Measured Using the NIH Stroke Scale Between Baseline and Post- Ablation (Pre-Discharge Visit) and at 12 Months Post-Ablation Procedure		
At Discharge:		
Mean (SEM / SD)	0.0 (0.02/0.32)	0.0 (0.02/0.30)
Median	0.0	0.0
Min, Max	-1, 3	-2, 2
N (N Missing)	222 (21)	216 (23)
At 12 Months:		
Mean (SEM / SD)	-0.1 (0.03/0.38)	-0.1 (0.02/0.36)
Median	0.0	0.0
Min, Max	-4, 1	-3, 0
N (N Missing)	212 (31)	214 (25)
Time to Achieve Initial PVI at Index Procedure (minutes), Defined as Time of Delivery of First RF Ablation with the Assigned Ablation Catheter Until Confirmation of PVI		

Mean (SEM / SD)	69.4 (2.28/35.15)	65.7 (1.95/29.89)
Median	56.5	56.0
Min, Max	21, 218	24, 192
N (N Missing)	238 (5)	235 (4)
Total Treatment Device Time (minutes), Defined as Time of Delivery of First RF Ablation with the Assigned Ablation Treatment Catheter to Removal of the Treatment Catheter		
Mean (SEM / SD)	91.4 (3.94/60.91)	83.1 (2.22/33.99)
Median	75.0	71.0
Min, Max	22, 802	30, 196
N (N Missing)	239 (4)	235 (4)
Total Number of RF Ablations Per Procedure		
Mean (SEM / SD)	71.1 (2.58/39.78)	74.2 (2.16/32.95)
Median	63.0	67.5
Min, Max	11, 264	17, 279
N (N Missing)	238 (5)	232 (7)
Total Fluid Infused Through the Assigned Ablation Catheter (mL)		
Mean (SEM / SD)	785.2 (22.83/351.5)	332.2 (7.88/120.8)
Median	721.7	307.0
Min, Max	3.8, 2095	57.0, 800.0
N (N Missing)	237 (6)	235 (4)
Number of Re-Hospitalizations Due to Atrial Fibrillation Recurrence After Blanking Period		
Mean (SEM / SD)	0.1 (0.02/0.26)	0.1 (0.02/0.29)
Median	0.0	0.0
Min, Max	0.0, 2.0	0.0, 2.0
N (N Missing)	243 (0)	239 (0)
0 Re-Hospitalization	229/243 (94.2%)	221/239 (92.5%)
1 Re-Hospitalization	13/243 (5.3%)	17/239 (7.1%)
2 Re-Hospitalizations	1/243 (0.4%)	1/239 (0.4%)

AF=Atrial Fibrillation, AFL=Atrial Flutter, AT=Atrial Tachycardia, CEC=Clinical Events Committee, NIH=National
Institute of Health, PV=Pulmonary Vein, PVI=Pulmonary Vein Isolation, QOL=Quality of Life, RF=Radiofrequency Min=Minimum, Max=Maximum, SEM=Standard Error of the Mean, SD=Standard Deviation
Notes: N=Number of subjects in the Intent-to-Treat Population. n=Number of subjects in the specific category. Percentages are calculated as 100 x (n/N).
[1] The top four specific secondary endpoints were evaluated for superiority over Control using a priori hierarchical hypotheses with a two-tailed alpha of 0.05, and testing stopped when the first non-significant result was reached.

iii. Blinding Assessment

The DIAMOND AF trial is a randomized, controlled, single-blind study. The success of subject blinding to treatment assignment was evaluated by asking subjects whether

they know they were in which treatment group at the 12-month follow-up visit. **Table 30** summarizes the blinding assessment results. In both treatment groups, majority of subjects did not know the treatment assignment.

Table 30. Blinding Assessment

Number of Subjects (Percentage)	**Which Treatment Group Does the Subject Believe He/She was Assigned To? (At 12-Month Follow-up Visit)**			
Actual Treatment Group Assignment	**Does Not Know**	**Control Device**	**Investigational Device**	**Total**
Control	121 (53.1%)	49 (21.5%)	58 (25.4%)	228
Investigational	120 (53.3%)	11 (4.9%)	94 (41.8%)	225
Total	241	60	152	453*
*Of all 455 subjects who completed the 12-month visit, 453 provided a response to this blinding question.				

3. Subgroup Analyses

Both primary safety endpoint results and primary effectiveness endpoint results were consistent by geography. Additional subgroup analyses also show consistency of the primary outcomes across gender and age (< 65 vs. ≥ 65 years).

4. Pediatric Extrapolation

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

D. 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 88 investigators of which none were full-time or part-time employees of the sponsor and 2 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: 1
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 2

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

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

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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness outcomes of the DIAMOND-AF study demonstrate a reasonable assurance that the DiamondTemp Ablation System is effective for the treatment of symptomatic drug refractory recurrent paroxysmal atrial fibrillation.

The pivotal study met its primary effectiveness objective. The primary effectiveness endpoint success was observed in in 184 (75.7%) Control (TactiCath) subjects and 189 (79.1%) DiamondTemp subjects. The lower two-sided 95% confidence limit of -4.2% exceeded the non-inferiority margin of -12.5% and the primary effectiveness objective was met ($p<0.0001$). The results demonstrate that the DiamondTemp Ablation System is as effective as an approved device for the intended use.

For patients treated with the DiamondTemp ablation system, the observed freedom from documented AF, AT and AFL episodes following the blanking period through 12 month in the absence of class I and III anti-arrhythmic drug therapy was 59.4%. The estimate is in line with the expected success from contemporary PAF catheter ablation treatment.

Treated subjects in both groups gained clinically meaningful quality of life improvement (QoL) from baseline to 6 and 12 months post ablation as measured by the AFEQT assessment.

There are some uncertainties in the assessment of benefit due to moderately low rhythm monitoring compliance for detecting treatment failures. While rhythm monitoring compliance was similar between the two treatment groups, poor adherence to the rhythm monitoring schedule could have inflated the primary effectiveness endpoint estimates.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in the clinical study conducted to support PMA approval as described above. The safety of the DiamondTemp Ablation System for the treatment of drug refractory symptomatic paroxysmal atrial fibrillation was assessed by comparing to a marketed open irrigated contact force sensing catheter in the DIAMOND-AF Clinical Study.

Of the 243 subjects randomized to the Control group (TactiCath), 16 subjects (6.6%) had a CEC adjudicated adverse event that contributed to the primary safety endpoint. Of the 239 subjects enrolled/randomized to the DiamondTemp group, 8 subjects (3.3%) had a CEC adjudicated adverse event that contributed to the primary safety endpoint. These events in the DiamondTemp group included: cardiac tamponade/perforation, phrenic nerve paralysis, transient ischemic attack, vagal nerve injury, and vascular access complications.

The difference in the primary safety endpoint freedom rate between the two treatment groups was 3.24% (95% CI: -1.32% to 7.79%), and the lower two-sided 95% confidence limit of -1.32% exceeded the predetermined non-inferiority margin of -6.5%. The study met its primary safety objective, and the results demonstrate that the DiamondTemp Ablation System is as safe as an approved device for the intended use.

There were no unanticipated adverse device effects. The nature, frequency, and severity of the procedural complications observed in the study were in line with the published literature of catheter ablation for the treatment of paroxysmal atrial fibrillation. Other adverse events reported during the study did not raise significant concerns for a safety signal.

These data provide a reasonable assurance that the DiamondTemp Ablation System is safe for the treatment of symptomatic drug refractory recurrent paroxysmal atrial fibrillation.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in the clinical study conducted to support PMA approval as described above. For patients with symptomatic

paroxysmal atrial fibrillation refractory to the standard of care rhythm control pharmacological therapy, ablation treatment with the Medtronic DiamondTemp Ablation System resulted in freedom from recurrence of atrial arrhythmia for the majority of patients.

The probable risks of the device are also based on data collected in the clinical study conducted to support PMA Supplement approval as described above. The observed severity, types, and rates of harmful events associated with using the study catheters to treat symptomatic drug refractory paroxysmal atrial fibrillation are well in line with the risks associated with the approved device type for the intended use.

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

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for catheter ablation treatment of paroxysmal AF with the DiamondTemp Ablation System.

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.

XIII. CDRH DECISION

CDRH issued an approval order on January 27, 2021. The final clinical conditions of approval cited in the approval order are described below.

> **The DIAMOND AF PAS** is a global, prospective, non-randomized, single-arm, observational, multi-center study to evaluate the long-term effectiveness and safety of atrial ablation with the DiamondTemp™ Ablation System. The principle PAS design and analyses are per agreement dated January 25, 2021. A total of up to 175 patients aged 18 years or older will be enrolled worldwide over an enrollment period of 18-24 months with at least 50% of enrollment in the United States. Patients from the DIAMOND AF Study may be approached and consented for continued follow-up in the PAS. Follow up clinical data will be collected at 3 months, 6 months, 12 months, 24 months and 36 months. The primary objectives will be: (1) Estimate the 36-month freedom from atrial fibrillation (AF) recurrence using the DiamondTemp™ Ablation System; (2) Estimate the serious device or serious procedure related adverse events for catheter ablation using the DiamondTemp™ Ablation System through 12 months. The secondary objectives will obtain additional data for the DiamondTemp™ Ablation System as follows: (1) characterize the DiamondTemp™ ablation procedure; (2)

estimate the change in Quality of Life through 36 months; and (3) Estimate the 12 and 24-month freedom from AF/AFL/AT recurrence using the DiamondTemp™ Ablation System.

From the time of study protocol approval, you must meet the following timelines for the DIAMOND AF PAS:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months
- Submission of Final study report: 3 months from study completion (i.e. last subject, last follow-up date)

In addition, you must submit separate periodic reports on the progress of the DIAMOND AF PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports (i.e., every 3 months), in addition to your periodic (6-months) PAS Progress Reports, until FDA notifies you otherwise.

For all other condition of approval studies, you must submit separate PAS Progress Reports for each study, every six (6) months for the first two (years) and annually thereafter, unless otherwise specified by FDA.

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

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. IEC 60601-1, *Medical electrical equipment – Part 1: General requirements for basic safety and high frequency accessories*
   IEC 60601-2-2, *Medical electrical equipment – Part 2-2: Particular requirements for safety and essential performance of high frequency surgical equipment and high frequency accessories*
   IEC 60601-1-2, *Medical electrical equipment Part 1-2: General requirements for safety and essential performance – Collateral standard: Electrical compatibility – requirements and tests*