Clinical Investigation Plan

Safety and Effectiveness of TactiFlex™ Ablation Catheter, Sensor Enabled™ (TactiFlex SE) for the Treatment of Drug Refractory, Symptomatic, Paroxysmal Atrial Fibrillation (TactiFlex PAF IDE Trial)

May 29, 2020

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Clinical Investigation Plan

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TactiFlex PAF IDE
Safety and Effectiveness of TactiFlex Ablation Catheter, Sensor Enabled (TactiFlex SE) for the Treatment of Drug Refractory, Symptomatic, Paroxysmal Atrial Fibrillation

Version Number	[redacted]
Date	May 29, 2020
Planned Number of Sites and Region(s)	Up to 40 sites Worldwide
Clinical Investigation Type	Prospective, non-randomized multi-center clinical investigation. Design includes a main study and a separate substudy. Subjects in the main study are to be treated using the full range of ablation power settings in the IFU. Subjects in the substudy are to be treated in the upper end of the recommended ablation power settings (40-50 Watts).
Sponsor	Abbott [redacted]
CIP Author of Current Version	[redacted]
CRD Number	[redacted]

[redacted]

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SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

I have read and agree to adhere to the clinical investigation plan and all regulatory requirements applicable in conducting this clinical investigation.

Site Principal Investigator

Printed name:
Signature:
Date:

[redacted]

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COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, applicable Good Clinical Practices and regulations (e.g., US 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812 and OUS ISO14155:2011) and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical investigation will be approved by the appropriate Institutional Review Board (IRB)/Ethics Committee (EC) of the respective investigational site and by the applicable regulatory authorities (e.g., FDA, PMDA, MHRA, etc.).

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1.0 INTRODUCTION

This clinical investigation is intended to demonstrate the safety and effectiveness of the TactiFlex™ Ablation Catheter, Sensor Enabled™ (TactiFlex SE) for treating symptomatic drug-refractory paroxysmal atrial fibrillation. This clinical investigation will be conducted under an investigational device exemption (IDE) and is intended to support market approval of the TactiFlex SE catheter worldwide. Three hundred fifty-five (355) subjects will be enrolled at up to 40 investigational sites worldwide. This clinical investigation is sponsored by Abbott.

This clinical investigation will be conducted in accordance with this CIP. All investigators involved in the conduct of the clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

1.1 Background and Rationale

1.1.1 Background

It has been estimated that 33.5 million people have atrial fibrillation (AF) worldwide [1]. AF has a prevalence of approximately 3% in adults aged 20 years or older [2, 3]. Additionally, one in four middle-aged adults in the US and EMEA will develop AF in their lifetime [4, 5].

AF remains a major cause of stroke, heart failure, sudden death, and cardiovascular morbidity. In a meta-analysis of contemporary, well-controlled, randomized clinical trials in AF, the average annual stroke rate is 1.5% with an annualized death rate of 3% in anticoagulated AF patients [6]. A minority of these deaths are related to stroke, while sudden cardiac death and death from progressive heart failure are more frequent, emphasizing the need for interventions beyond anticoagulation [7, 8]. AF is also associated with high rates of hospitalization for AF management, treatment-associated complications, heart failure and myocardial infarction [9, 10]. Patients with AF have significantly reduced quality of life vs. healthy controls, experiencing a variety of symptoms including lethargy, palpitations, dyspnea, chest pain, sleeping difficulties, and mental distress [10-14] .

Treatment for AF includes thromboembolic risk management, heart rate control, and heart rhythm control, which includes cardioversion and catheter ablation. The 2014 AHA/ACC/HRS AF Guidelines, 2016 ESC AF Guidelines, and 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus on AF Ablation all provide a Class I recommendation (Level of Evidence: A) for catheter ablation to maintain sinus rhythm for patients with symptomatic, drug refractory, paroxysmal AF [15-17].

Contact force-sensing ablation catheter systems are a technology that is growing in adoption for AF ablation. These contact force-sensing catheter systems provide catheter operators additional feedback by allowing the operator to know how much force is being applied by the catheter tip on the cardiac tissue.

The TactiCath family of contact force-sensing catheters from Abbott has been studied extensively in human clinical trials [18-22]. The latest TactiCath™ contact force sensing catheter from Abbott is the TactiCath SE ablation catheter, which incorporates a magnetic sensor for tracking with the EnSite Precision Mapping System and utilizes a new handle and shaft to improve catheter handling. The TactiCath SE catheter is being investigated by the TactiSense clinical trial [23].

The flexible-tip ("flex-tip") family of ablation catheters (Therapy™ CoolFlex™, FlexAbility™, FlexAbility™ SE) from Abbott offers a tip design that is significantly different from the rigid-tip TactiCath family. While

[redacted]

both catheter families provide irrigating saline through 4-6 discrete holes at the distal tip, only the flex-tip family provides irrigating saline through an interlocking pattern of kerfs laser-cut into the side of the electrode that is both flexible and porous. The purpose of having the saline irrigated over a more widely distributed area is to produce a more uniform temperature profile, potentially increasing the efficiency of energy transfer [24] and reducing the risk of steam-pops [25]. The Therapy CoolFlex ablation catheter has been studied in humans for the treatment of typical atrial flutter [26] and the entire flex-tip family is indicated for the treatment of typical atrial flutter in the US. Outside of the US, the flex-tip family of catheters is indicated for treating cardiac arrhythmias and is used to treat AF. The safety and effectiveness of flex-tip catheters has been studied for the treatment of paroxysmal AF in a real-world setting through the ABLATOR patient registry [27].

The TactiFlex™ Ablation Catheter, Sensor-Enabled™ (TactiFlex SE) is the next generation design from Abbott, and it has several elements that are similar or identical to the FlexAbility SE and/or TactiCath SE ablation catheters. The contact force sensor, handle (uni- or bi-directional) and shaft are like TactiCath SE. Meanwhile, the porous flex-tip ablation electrode and therapy RF circuit are like FlexAbility SE. Unlike TactiCath SE and FlexAbility SE, TactiFlex SE has a second magnetic sensor that enables the force direction arrow and deflection/direction features in the EnSite Precision cardiac mapping system (v2.5).

1.1.2 Rationale for Conducting this Clinical Investigation

The TactiFlex PAF IDE study will be the first time that the TactiFlex SE ablation catheter has been used in humans. The goal of this clinical trial will be to demonstrate the safety and effectiveness of this catheter for the treatment of paroxysmal AF in the worldwide patient population.

2.0 CLINICAL INVESTIGATION OVERVIEW

2.1 Clinical Investigation Objective

2.1.1 Primary Objective

The primary objective of the TactiFlex PAF IDE clinical trial is to demonstrate that ablation with the TactiFlex™ Ablation Catheter, Sensor-Enabled™ (TactiFlex SE), in conjunction with a compatible RF generator and three-dimensional mapping system, is safe and effective for the treatment of drug refractory, symptomatic paroxysmal atrial fibrillation (PAF) when following standard electrophysiology mapping and radiofrequency (RF) ablation procedures.

2.1.2 Secondary Objectives

The TactiFlex PAF IDE clinical trial has two secondary objectives:

1. To provide supporting data for the safety and effectiveness of using TactiFlex SE at 40-50 Watts in the left atrium as part of an AF ablation procedure.
2. To provide supporting data for the safety and effectiveness of using TactiFlex SE to treat cavo-tricuspid isthmus (CTI)-dependent (or "typical") atrial flutter (AFL) through the ablation of the CTI in the right atrium. This data may be used to support an expanded indication for the treatment of CTI-dependent AFL.

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2.2 Devices to be Used in the Clinical Investigation

2.2.1 Name of the Device(s) Under Investigation

The components of the ablation system (**Table 1**) to be used in this clinical trial include investigational and commercial devices. In the United States, some commercial devices will be considered investigational when used in this study, while others will be used as commercially indicated. The *Instructions for Use* document for each device and/or *Investigator's Brochure* document for this clinical investigation should be referenced, as appropriate. The list of devices used in the study and their respective model numbers are listed in **Table 1**. In all geographies, the investigational EnSite IDE Display Workstation will be delivered to each clinical site and initially installed by an Abbott employee.

The Ampere RF Generator and TactiSys Quartz Equipment will be obtained by study sites through their usual commercial channels.

United States Only

A label indicating each device is considered part of an investigational system for use in the TactiFlex PAF IDE trial will be affixed by Abbott personnel to the Ampere generator and TactiSys Quartz equipment.

Outside the United States Only

The models of the Ampere™ RF Generator and Cool Point™ Irrigation pump that are market-released outside of the United States have a different upper power limit (100 Watts) and default irrigation flowrate (17 mL/min) vs. the market-released US models. For this clinical investigation, the recommended irrigation flowrate is 13 mL/min and the power setting must not exceed 50 Watts. Refer to the *Instructions for Use* document for the TactiFlex SE catheter for more information.

Table 1. Study Devices

Device Name	Model No. (ZFIN No.) [4]	Serialized / Lot-Controlled	Manufacturer	Region	Investigational or Market Released
TactiFlex Ablation Catheter, Sensor Enabled	A-TFSE-DD-CLIN A-TFSE-DF-CLIN A-TFSE-FF-CLIN A-TFSE-FJ-CLIN A-TFSE-JJ-CLIN A-TFSE-D-CLIN A-TFSE-F-CLIN A-TFSE-J-CLIN	Serialized	St. Jude Medical [1]	WW	Investigational
TactiSys™ Quartz Equipment	PN-004 400	Serialized	St. Jude Medical [2]	US	Commercial Device – Investigational when used as part of the study
				OUS	Commercial
Ampere™ Generator (Software v1.0.6 or greater)	H700488	Serialized	St. Jude Medical [2]	US	Commercial Device – Investigational when used as part of the study
	H700489	Serialized	St. Jude Medical [2]	OUS	Commercial

[redacted]

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Device Name	Model No. (ZFIN No.)[4]	Serialized / Lot-Controlled	Manufacturer	Region	Investigational or Market Released
TactiSys™ Quartz, TactiFlex™ Ablation Catheter SE RF Cable	TSQ-RF-TF-CBL-CLIN	Serialized	St. Jude Medical [2]	WW	Investigational
Cool Point™ Irrigation Pump (Software v24 or greater)	IBI-89003	Serialized	Irvine Biomedical, Inc., a St. Jude Medical Company	US	Commercial
	85784	Serialized	Irvine Biomedical, Inc., a St. Jude Medical Company	OUS	Commercial
EnSite™ Precision Cardiac Mapping System	Includes models listed below	See below	See below	WW	See status associated with models listed below
EnSite IDE Display Workstation (Investigational Software Velocity v5.5/Precision v2.5 and associated licensed modules)	ESDWS-CLIN1	Serialized	St. Jude Medical [2]	WW	Investigational
EnSite Velocity Amplifier	100014514	Serialized	St. Jude Medical [2]	WW	Commercial
EnSite Precision Surface Electrode Kit	EN0020-P	Lot-Controlled	St. Jude Medical [3]	WW	Commercial
Other EnSite Accessories	Various	Various	Various	WW	Commercial
EnSite Precision Module, Sensor Enabled	H702470, Includes models listed below	Serialized	St. Jude Medical [2]	US	Commercial
	H702473, Includes models listed below	Serialized	St. Jude Medical [2]	OUS	Commercial
EnSite Precision™ Field Frame	H702469	Serialized	St. Jude Medical [2]	WW	Commercial
EnSite Precision™ Link, Sensor Enabled™	H702475 (ZFINs: 100133139, or 100142361)	Serialized	St. Jude Medical [2]	WW	Commercial
EnSite Precision™ Patient Reference Sensor	H702492	Lot-Controlled	St. Jude Medical [2]	WW	Commercial
Other EnSite Precision Module Accessories	Various	Various	Various	WW	Commercial

1. 5050 Nathan Lane N | Plymouth, MN | USA
2. One St. Jude Medical Drive | St. Paul, MN | USA
3. Costa Rica Ltda.
4. If specific ZFIN is required.

2.2.2 Intended Indication for Use

The TactiFlex™ Ablation Catheter, Sensor Enabled™ (TactiFlex SE) is indicated for use in cardiac electrophysiological mapping and for the treatment of drug-refractory recurrent symptomatic paroxysmal atrial fibrillation, when used in conjunction with a compatible radiofrequency generator and three-dimensional mapping system.

[redacted]

2.2.3 Description of the Device(s) Under Investigation

2.2.3.1 TactiFlex™ Ablation Catheter, Sensor Enabled™

The TactiFlex™ Ablation Catheter, Sensor Enabled™ (TactiFlex SE) is designed to facilitate electrophysiological mapping of the heart chambers and to transmit RF current to the catheter flexible tip electrode for intracardiac ablation purposes. The catheter is used in conjunction with a RF generator, an irrigation pump, and a dispersive pad (indifferent patch electrode) when ablating. TactiFlex SE is compatible with introducers or sheaths with a minimum diameter of 8.5 F. TactiFlex SE is a sterile, single use catheter with a 7.5 F shaft and an 8 F distal section. It is constructed of thermoplastic elastomer material and noble metal electrodes.

TactiFlex SE has a fiber-optic based contact force sensor and a six degree-of-freedom magnetic sensor for position and orientation. It has a fluid lumen connected to an open-irrigated tip electrode for saline irrigation during the ablation procedure (**Figure 1**). For both uni-directional (**Figure 2**) and bi-directional catheters (**Figure 3**), the tip curvature is manipulated by the control mechanism located on the handle at the catheter's proximal end. To adjust the curve of the distal tip on the uni-directional catheter, the thumb control located on the handle may be pushed or pulled. To adjust the curve of the distal tip on the bi-directional catheter, the actuator may be used to deflect the catheter in either direction. The catheter interfaces with standard recording equipment and a compatible RF generator via the TactiSys Quartz Equipment using the optical connector and the 19-pin electrical connector on the catheter. Connection to EnSite Precision magnetic sensor equipment is made using the 10-pin electrical connector on the catheter. The catheters are available in eight distal curve shapes across the two handle types.

Please refer to the IFU for additional information regarding the device used in this clinical investigation.

[redacted]

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Figure 1. Schematic View of the TactiFlex SE Tip

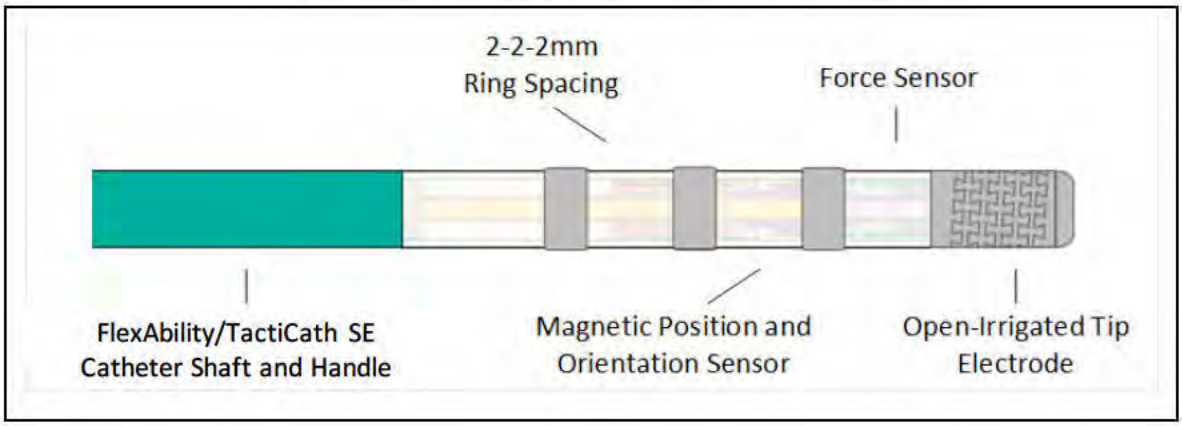


Figure 2. Uni-Directional TactiFlex SE

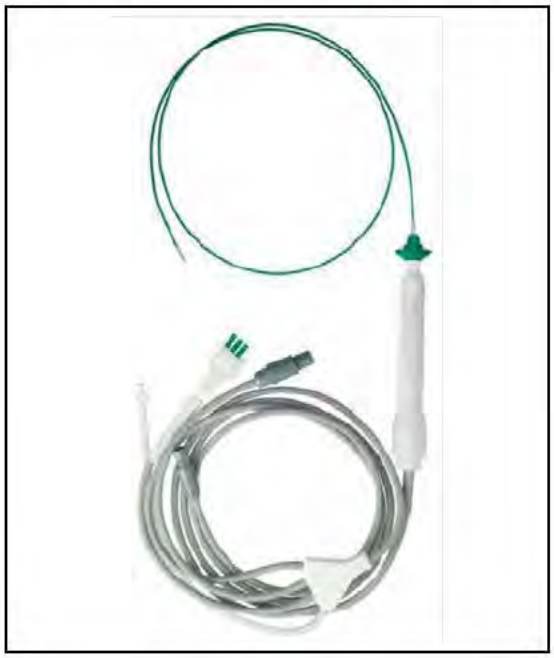
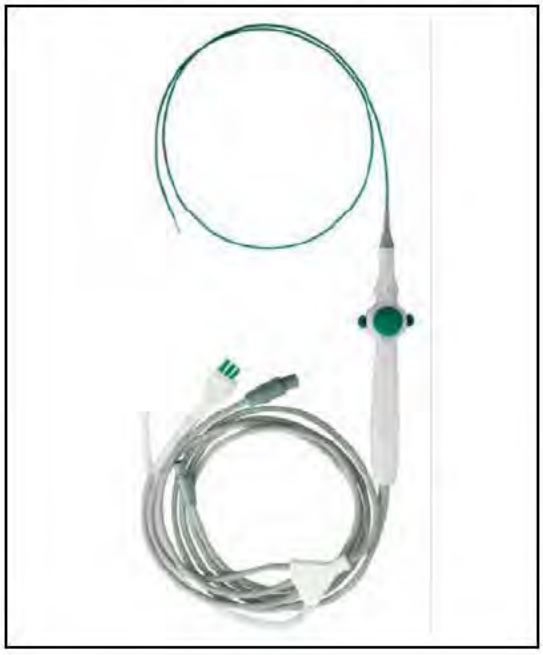


Figure 3. Bi-Directional TactiFlex SE



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2.2.3.2 EnSite™ IDE Display Workstation

An investigational version of the EnSite Precision Cardiac Mapping System will be used for this clinical study. This investigational software was created from the base EnSite Velocity v5.2.1 / Ensite Precision v2.2 commercial software (K172396), with the following changes:

[redacted]

The investigational software will be deployed through the EnSite IDE Display Workstation (Model ESDWS-Clin1).

[redacted]

Please refer to the IFU for additional information regarding the device used in this clinical investigation.

2.2.3.3 TactiSys™ Quartz, TactiFlex™ Ablation Catheter SE RF Cable

The TactiSys™ Quartz, TactiFlex™ Ablation Catheter SE RF Cable (TactiFlex™ RF Cable, TSQ-RF-TF-CBL-CLIN) is an investigational cable that will be used to connect the TactiSys™ Quartz Equipment to the Ampere™ Generator. The Ampere™ Generator is responsible for generating RF energy to transmit to the TactiFlex™ SE catheter. The TactiSys™ Quartz Equipment is responsible for calculating the contact force from the fiber-optic based sensor and is directly connected to the TactiFlex™ SE catheter through the optical connector and the 19-pin electrical connector on the catheter. The Ampere™ Generator transmits RF current to a contact force catheter through the TactiSys™ Quartz equipment via a RF cable. The current contact force catheters (TactiCath SE and TactiCath Quartz), have a RF cable that informs Ampere which default ablation parameters to use. [redacted]

[redacted]

2.2.4 Summary of Preclinical Studies

A summary of the preclinical studies for the investigational devices may be found in the Investigator's Brochure (OUS) or in the Report of Prior Investigations (US).

2.2.5 Device Handling

Sponsor requires all investigational products to be stored according to the labeling and *Instructions for Use* in a secure area to prevent unauthorized access or use. This applies to the following devices Worldwide:

1. EnSite IDE Display Workstation
2. TactiFlex SE catheters
3. RF cables (Model TSQ-RF-TF-CBL-CLIN)

The market-released TactiSys Quartz Equipment and Ampere generator can be stored per standard practice at each hospital.

3.0 CLINICAL INVESTIGATION DESIGN

This is a prospective, non-randomized, multi-center pivotal clinical trial to evaluate the safety and effectiveness of ablation with the TactiFlex SE catheter for the treatment of PAF compared to pre-determined performance goals. The study design includes a substudy to assure that there will be at least 50 subjects ablated at the high-end of the ablation power setting recommendations in the investigational *Instructions for Use* document. Subjects in the HSP (High Standard Power) substudy are to undergo the same study procedures as subjects in the main study, except that ablation power settings of 40-50 Watts are to be used in the left atrium, unless there is a medical reason to use a lower power. Operators will be assigned to either the main study or the HSP substudy based on the ablation power settings they currently use in their standard practice. Subjects will be enrolled in either the main study or the substudy at the point of consent based on the operator that is expected to perform their ablation procedure. After the substudy has enrolled 50 subjects, or if the Sponsor has provided written permission, HSP operators may transition to the main study and treat main study subjects. No site may enroll more than 10 subjects (20%) in the HSP substudy without Sponsor pre-approval and at least 25 HSP substudy subjects (50%) must be from the United States.

Up to 40 sites worldwide will participate in the TactiFlex PAF IDE clinical study. The TactiFlex IDE Clinical Study will enroll a total of 355 subjects. Fifty (50) subjects will be enrolled in the HSP Substudy and 305 subjects will be enrolled in the Main Study. No center may contribute more than 20% (*N*=61) of the total number of enrollments in the main study without Sponsor pre-approval. At least 50% (*N*=153) of the subjects will be from the US.

[redacted] Subjects will be followed for 12-months after their initial ablation procedure. The primary and secondary endpoints will be evaluated when all subjects have completed their 12-month follow-up visit. [redacted]

[redacted] All adverse events (AEs), with logical exceptions, from the point of enrollment through study exit will be documented and reported. A Clinical Event Committee (CEC) will be used to adjudicate all AEs that are determined by the Sponsor to potentially meet the criteria of 1) a serious AE and/or 2) an AE related to the investigational devices or ablation procedure.

The clinical investigation has been designed to involve as little pain, discomfort, fear, and any other foreseeable risk as possible for subjects. Refer to the Risks Analysis section of this clinical investigation plan for details.

3.1 Clinical Investigation Procedures and Follow-up Schedule

The visit schedule for subjects is shown in **Figure 5**. Once eligibility is confirmed, the subject will undergo a study ablation procedure for treatment of their PAF condition. A blanking period of 90-days will be employed after the initial ablation procedure, followed by a 9-month evaluation period. The total follow-up period will be for 12 months. Medication adjustments, cardioversions, and one repeat ablation procedure may be performed in the blanking period without being considered a primary effectiveness endpoint failure (repeat ablation for AF must be performed 31-80 days after the initial procedure). Subjects must be off Class I and III antiarrhythmic drugs (AADs) after the blanking period, unless clinically justified. Follow-up assessments will occur either in-person at the clinic or via phone contact after the procedure. The scheduled follow-up visits will occur before the patient leaves the hospital and then at 7-days (phone call), 5-weeks (phone call), 3-months (in-person visit), 6-months (phone call), and 12-months (in-person visit) after the initial procedure. The subject will be exited from the trial after completing their 12-month follow-up visit.

[redacted]

Clinical Investigation Plan

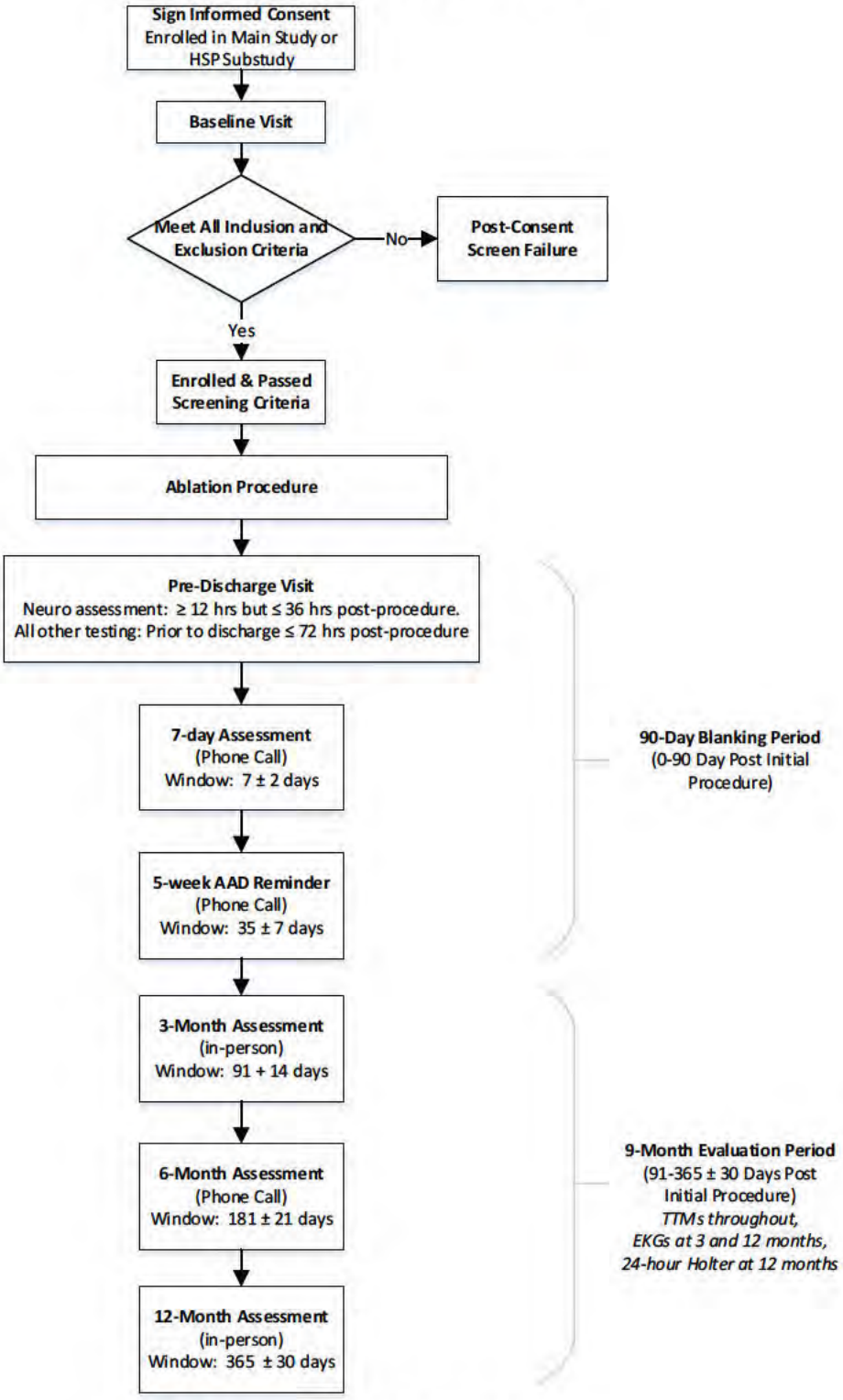

Figure 5. Study Flow Diagram

[redacted]

3.2 Measures Taken to Avoid and Minimize Bias

Multiple measures will be taken to avoid and minimize bias in this clinical investigation. First, TactiFlex PAF IDE is a prospective clinical investigation in which the outcome is unknown at the time of enrollment and all subjects must meet the defined eligibility criteria to minimize selection bias. Next, guidance will be provided to sites regarding data collection for questionnaires and the post-procedure follow-up phone calls to be performed at 7-days, 5-weeks, and 6-months post-procedure. Additionally, case report forms for data collection will be provided to sites, which will minimize inter-observer variability.

Evaluation of primary endpoint data will be performed by an independent core laboratory and Clinical Events Committee (CEC). Collected electrocardiogram (ECG), trans-telephonic monitoring (TTM), and 24-hour Holter data from sites will be evaluated by a physician at a core laboratory to determine AF recurrence for subjects. To ensure consistent monitoring for arrhythmia recurrence across the subject population, it is required (as permitted by local regulations) that either the core lab or site personnel contact the subjects to help them perform each scheduled TTM transmission and verify that the transmission has been received by the core lab.

A CEC made up of physicians who are not investigators in the trial will be used to adjudicate all AEs that are determined by the Sponsor's Safety group to potentially meet the criteria of 1) a serious AE and/or 2) an AE related to the investigational devices or ablation procedure. To minimize bias, only the core lab and the CEC's adjudication of the collected data will be used for the analysis of the primary safety endpoint.

Protocols are also in place to minimize lost to follow-up subjects (**Section 5.5.1**). Sensitivity analyses will be performed demonstrating the impact missing data may have on the trial.

An independent Data Safety Monitoring Board (DSMB) will be established (**Section 10.9.3**) and serve in an advisory role to the Sponsor to ensure safety by reviewing cumulative data from the clinical investigation at prescribed intervals for the purpose of safeguarding the interests of enrolled subjects and those patients yet to be enrolled, as well as the continuing validity and scientific merit of the clinical investigation.

3.3 Suspension or Early Termination of the Clinical Investigation

The Sponsor reserves the right to discontinue the clinical investigation at any stage or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Unanticipated (serious) adverse device effect (e.g., UADE, USADE) occurs and it presents an unreasonable risk to the participating subjects
- An oversight committee (e.g., Steering Committee, DSMB) makes a recommendation to stop or terminate the clinical investigation (such as higher frequency of anticipated adverse device effects)
- Further product development is cancelled.

Should the clinical investigation be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements. The investigator shall return all clinical investigation materials (including devices) to the

[redacted]

Sponsor and provide a written statement to the IRB/EC (if applicable). All applicable clinical investigation documents shall be subject to the same retention policy as detailed in **Section 11.5** of the CIP.

An IRB/EC or regulatory authority may suspend or prematurely terminate participation in the clinical investigation at the investigational site(s) for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

If the Sponsor suspends or prematurely terminates the clinical investigation at an individual site in the interest of safety, the Sponsor will inform all other Investigators.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements for following the subjects enrolled in the clinical investigation, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate.

4.0 ENDPOINTS

4.1 Primary Endpoints and Rationale

4.1.1 Primary Safety Endpoint

The primary safety endpoint is the rate of device and/or procedure-related serious adverse events with onset within 7-days of any ablation procedure that uses the TactiFlex SE catheter (initial or repeat procedure performed 31-80 days of initial procedure) that are defined below:

- Atrio-esophageal fistula[1]
- Cardiac tamponade/perforation[1]
- Death
- Heart block
- Myocardial infarction
- Pericarditis
- Phrenic nerve injury resulting in diaphragmatic paralysis
- Pulmonary edema
- Pulmonary vein stenosis[1]
- Stroke/cerebrovascular accident
- Thromboembolism
- Transient ischemic attack
- Vagal nerve injury/gastroparesis
- Vascular access complications (including major bleeding events[2])

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1. Atrio-esophageal fistula, cardiac tamponade/perforation and pulmonary vein stenosis will be evaluated through 12-months.
2. Bleeding is a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in hematocrit.

These events must meet the criteria listed in **Appendix II** to be included in the primary endpoint as adjudicated by the Clinical Events Committee (CEC).

The performance goal for the Primary Safety Endpoint for this clinical trial [redacted] = 12.9%. [redacted]

[redacted] Additional details are provided in the Statistical Analysis Plan.

4.1.1.1 Rationale for Selection of the Primary Safety Endpoint

Peri-procedural serious adverse events (SAEs) that are adjudicated as being related to the procedure and/or the device are being assessed in the primary safety endpoint. The majority of the pre-identified SAEs that require reporting in this study occur within the first 7-days following an ablation procedure. It has become industry standard to report adverse events with onset within the first 7-days of an ablation procedure for AF. However, symptoms of PV stenosis and atrial-esophageal fistula may not be apparent in the acute period following the procedure. Notably, the 2004 FDA Guidance entitled "Clinical Study Designs for Percutaneous Catheter Ablation for Treatment of Atrial Fibrillation", dated January 9, 2004 [32] recommends that PV stenosis be assessed at 3-months and 1-year post-ablation. Additionally, cardiac tamponade/perforation may be related to the device/ procedure even though it may not be discovered within the 7-day post-procedure period. Therefore, symptoms indicative of PV stenosis, atrial-esophageal fistula, and cardiac tamponade/perforation be assessed throughout the clinical investigation and appropriate follow-up testing be conducted as clinically indicated.

[redacted]

[redacted]

4.1.2 Primary Effectiveness Endpoint

The primary effectiveness endpoint for this clinical trial is freedom from documented (symptomatic or asymptomatic) AF/AFL/AT episodes of >30 seconds duration that are documented by 12-lead ECG, transtelephonic monitoring (TTM) or Holter monitor after the initial catheter ablation procedure through 12-months of follow-up (9 months after a 90-day blanking period).

AF/AFL/AT recurrence during the 90-day blanking period (≤90 days post-initial procedure) will not be considered a treatment failure. One repeat procedure will be allowed for ablation of AF/AFL/AT [redacted]

recurrence 31-80 days after the initial procedure and will not be considered a treatment failure. Failure to achieve acute procedural success (confirmation of entrance block after a 20-minute minimum waiting period) during the last ablation procedure[1] with the TactiFlex SE catheter will constitute failure to achieve this endpoint. After the 90-day blanking period, use of Class I or III AADs will not count as a therapy failure provided that only previously failed Class I or III AADs are taken at doses that do not exceed the previously failed dose.

AF/AFL/AT recurrence will only be assessed by 12-lead ECG, TTM, and Holter monitoring devices for assessment of this primary endpoint so that all subjects are monitored equally with devices of the same sensitivity and specificity (recurrence data collected from other devices such as pacemakers, ICDs, or ICMs will not be included in the assessment). ECG, TTM, and Holter data collected from sites will be evaluated by a core laboratory to ensure independent and unbiased assessment of AF/AFL/AT recurrence for endpoint analysis.

There are multiple situations in which subjects will be considered primary effectiveness endpoint failures:

- If the subject fails to achieve acute procedural success, defined as confirmation of entrance block in all pulmonary veins after a minimum waiting period of 20-minutes, during last ablation procedure performed with the TactiFlex SE catheter, or
- If documented AF/AFL/AT recurrence (>30 second episode) occurs at any time after the blanking period (>90 days after the initial procedure), or
- If the subject requires a repeat procedure for the treatment of AF >80 days after the initial procedure, the subject will be considered an effectiveness endpoint failure regardless of documentation of a >30 second AF/AFL/AT episode, or
- If the subject requires a second repeat AF ablation procedure ≤80 days after the initial procedure, or
- Any use of a new class I or III AAD for AF after the blanking period, or
- Any use of a class I or III ADD for AF at a dose higher than that previously failed by the patient, or
- If the subject requires a cardioversion (electrical or pharmacological) for the treatment of AF after the blanking period, or
- If the subject has a continuous atrial arrhythmia throughout a 12-lead ECG recording after the blanking period indicating AF/AFL/AT recurrence, this will be considered sufficient documentation of recurrence unless there is evidence that the recorded arrhythmia is short-lived and less than 30 seconds as determined by the investigator, or
- Any ablation in the left atrium using an ablation catheter other than TactiFlex SE.

Cavotricuspid isthmus (CTI)-dependent AFL that occurs alone either during or after the blanking period will be considered an exception to being considered a recurrence, as CTI-dependent AFL is easily treated with cavotricuspid isthmus ablation and is not an iatrogenic arrhythmia following a left atrial ablation procedure for AF. Occurrence of CTI-dependent AFL confirmed by entrainment maneuvers that occurs at any time during the follow-up period and is ablated, will not be considered a primary effectiveness endpoint failure.

The performance goal (PG) is set at 50% based on the chronic acceptable success rate for paroxysmal AF at 12-months in the 2017 Consensus Statement [17]. The 50% chronic acceptable success rate

[1] For subjects that have a repeat ablation procedure ≤80 days after the initial procedure, only failure to achieve acute procedural success during the repeat procedure will contribute to primary effectiveness endpoint.

[redacted]

assumes that the effectiveness endpoint definition includes effectiveness failure for any documented (symptomatic or asymptomatic) AF/AFL/AT episode of >30 seconds in duration.

4.1.2.1 Rationale for Selection of the Primary Effectiveness Endpoint

The guideline published by the 2017 Consensus Statement [17] was referred to when defining the primary effectiveness end-point for this clinical investigation. The following criteria were defined from this document for use in this clinical investigation: the definition of detectable AF defined as AF/AFL/AT of at least 30 seconds duration when assessed with ECG monitoring; an acceptable chronic success rate of 50% for PAF.

Counting the use of new or higher than previously failed doses of AADs after the blanking period as effectiveness failures is consistent with the primary effectiveness endpoint recommendations in the FDA Guidance on Clinical Study Designs for Percutaneous Catheter Ablation for the Treatment of Atrial Fibrillation [32].

4.2 Powered Secondary Endpoints

Type I error among secondary endpoints will be controlled using appropriate statistical methodology as outlined in the Statistical Analysis Plan.

4.2.1 AAD-Free Secondary Effectiveness Endpoint

The AAD-Free Secondary Effectiveness Endpoint has the same definition as the Primary Effectiveness Endpoint, except that any use of Class I or III AADs after the 90-day blanking period will count as a therapy failure in this analysis.

4.2.2 Single-Procedure Secondary Effectiveness Endpoint

The Single-Procedure Secondary Effectiveness Endpoint has the same definition as the Primary Effectiveness Endpoint, except that any repeat ablation in the left atrium will count as a failure.

4.2.3 Symptomatic Secondary Effectiveness Endpoint

The Symptomatic Secondary Effectiveness Endpoint has the same definition as the Primary Effectiveness Endpoint, except that episodes of documented recurrence without documented evidence of symptoms after the 90-day blanking period will not count as a therapy failure in this analysis.

4.3 HSP Substudy Endpoints

The endpoints for the HSP substudy will be defined the same as the Primary and Secondary Endpoints for the main study. Results will be reported descriptively using summary statistics. No pre-specified hypothesis testing will be performed.

The following as-treated analyses will be performed using the Primary and Secondary Endpoint results from main study and HSP substudy subjects.

1. Results will be summarized separately for subjects that have time-averaged power settings of ≥40 Watts vs. <40 Watts in the left atrium.

[redacted]

2. Results will be summarized separately for subjects that have ≥50% vs. <50% of lesions in the left atrium with power settings ≥40 Watts.
3. Results will be summarized separately for subjects that have ≥25% vs. <25% of lesions in the left atrium with power settings ≥40 Watts.

4.4 Additional Data

The following additional data will be collected and reported using only summary statistics and no hypothesis tests with pre-specified criteria will be performed. These descriptive endpoints will be reported separately for main study subjects and HSP substudy subjects. An as treated analysis will be conducted using the Additional Data as described in the SAP.

1. Proportion of subjects who achieve acute procedural success during the initial ablation procedure, where acute procedural success is defined as confirmation of entrance block in all pulmonary veins after a minimum waiting period of 20-minutes.
2. Proportion of subjects with successful first-pass PV isolation during the initial ablation procedure, defined as confirmation of entrance block in all pulmonary veins following the initial minimum waiting period of 20-minutes.
3. Proportion of subjects who experience any adverse event (AE)
4. Proportion of subjects who experience any serious adverse event (SAE)
5. Proportion of subjects that experience any procedure- and/or ablation catheter-related adverse event (AE) throughout the 12-month follow-up period.
6. Proportion of subjects requiring one or more repeat AF ablations at 12 months following the initial AF ablation procedure.
7. Changes in EQ-5D-5L and AFEQT scores from baseline to follow up at 3, 6, and 12-months after the initial procedure.
8. Procedure data, including but not limited to, ablation data, mapping data, usage of HD Grid, usage of Automark, target contact force, power setting data, procedure time, fluoroscopy time, total RF time, time to perform initial PVI, and ablation lesions performed in addition to PVI.
9. Proportion of subjects treated for concomitant typical AFL with the TactiFlex SE catheter
10. Proportion of subjects treated for typical AFL with no recurrent AFL at 3, 6 and 12 months.
11. Proportion of subjects that received CTI ablation with the TactiFlex SE catheter.
12. Proportion of subjects that received CTI ablation that achieved bi-directional block.
13. Evaluation of procedure data to determine target contact force as assessed by AF/AFL/AT recurrence.
14. Evaluation of the relationship between ablation power with time to perform initial PVI.

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical investigation will enroll male and female subjects who have drug refractory, symptomatic, paroxysmal AF. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any investigation-specific procedures not considered standard of care.

[redacted]

5.2 Subject Screening and Informed Consent

5.2.1 Subject Screening

Potential patients presenting at the clinical sites will be fully informed about the clinical investigation, following the established Informed Consent process (described in **Section 5.2.2**). Once a duly dated and signed Informed Consent form is obtained, the clinical investigation-specific screening procedures may begin.

The following assessments may need to be performed after obtaining consent and prior to the procedure, as part of the screening process (further described in **Section 6.0**):

- Verification that a left atrial thrombus is not present on the day of or within one day of the ablation procedure (required for all subjects after consent, prior to procedure).
- Measurements for LVEF and LAD within 180 days of procedure, if not documented prior to consent and/or is not standard of care at the site.
- Electrocardiographic documentation of an AF episode within 12-months prior to informed consent/enrollment, if not already available in the patient's medical records. Documented evidence of an AF episode may be provided by a 12-lead ECG, Holter monitor, TTM, ICM, permanent pacemaker, or patch cardiac monitor. Documented evidence of the AF episode must either be continuous AF on a 12-lead ECG or include at least 30 seconds of AF on other ECG devices. Other forms of electrocardiographic documentation may be accepted at the approval of the Sponsor's Medical Director.

Subjects must be screened for clinical investigation eligibility by a member of the site's clinical investigation team previously trained to the CIP and will be entered into a site-specific screening log.

In case the subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject is considered a screening failure. The Site Principal Investigator or the delegated clinical investigation personnel will record the screening failure in the hospital records and on a screening log.

Patients meeting general inclusion criteria and no exclusion criteria will be asked to sign an Informed Consent form if they wish to participate in the clinical investigation. These patients will also be entered into the screening log.

Subject data will be collected following enrollment into the clinical investigation.

5.2.2 Informed Consent

A template informed consent form will be provided to each site by the Sponsor under separate cover for use in this clinical investigation. Site-specific language will be added to the template and approved by research personnel, the Sponsor, and governing IRB/EC prior for use in the trial.

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

[redacted]

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subject. Subjects may be compensated for time and travel directly related to the participation in the clinical investigation. The subject shall be provided with the Informed Consent form written in a language that is understandable to the subject and has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical investigation-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

Failure to obtain informed consent from a subject prior to clinical investigation enrollment should be reported to Sponsor within 5 working days and to the reviewing center's IRB/EC according to the IRB's/ EC's reporting requirements.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

5.2.2.1 Special Circumstances for Informed Consent

The following individual populations will be excluded from participation in this clinical investigation:

- Individuals without legal authority are excluded from the study population.
- Individuals under the age of 18 or age of legal consent are excluded from the study population.
- Individuals unable to read or write are excluded from the study population.
- Pregnant or breastfeeding women are excluded from the study population.

5.2.3 HIPPAA Authorization Requirement (US only)

In addition, an authorization for use and disclosure of the subject's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), must be obtained from the subject or their legally acceptable representative. This authorization may be part of the Informed Consent form, or a separate form.

5.3 Eligibility Criteria

5.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient, and determination by the investigator. If some of the clinical and laboratory tests are not included in site standard tests, they must be done after written informed consent is obtained, but before the subject has an ablation catheter inserted into their vasculature for an ablation procedure. Potential specific examples of this include the tests noted in in **Section 5.2.1** (LVEF, LAD, presence of thrombus, and electrocardiographic documentation of an AF episode within the prior 12-month period).

[redacted]

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Patients must meet ALL of the inclusion criteria to undergo the study procedures. If ANY of the exclusion criteria are met, the patient is excluded from the clinical investigation and cannot undergo the study procedures.

5.3.2 Inclusion Criteria

A patient will be eligible for clinical trial participation if he/she meets the following criteria:

1. Plans to undergo a catheter ablation procedure due to symptomatic PAF that is refractory or intolerant to at least one Class I or III antiarrhythmic drug.
2. Physician's note indicating recurrent self-terminating AF
3. One electrocardiographically documented AF episode within 12-months prior to informed consent/enrollment. Documented evidence of the AF episode must either be continuous AF on a 12-lead ECG or include at least 30 seconds of AF from another ECG device.
4. At least 18 years of age
5. Able and willing to comply with all trial requirements
6. Informed of the nature of the trial, agreed to its provisions and has provided written informed consent as approved by the Institutional Review Board/Ethics Committee (IRB/EC) of the respective clinical trial site.

5.3.3 Exclusion Criteria

A patient will be excluded from enrollment in the clinical trial if he/she meets any of the following criteria:

1. Persistent or long-standing persistent atrial fibrillation
2. Active systemic infection
3. Known presence of cardiac thrombus
4. Hypertrophic cardiomyopathy
5. Arrhythmia due to reversible causes including thyroid disorders, acute alcohol intoxication, and other major surgical procedures in the 90-day period preceding procedure
6. Myocardial infarction (MI), acute coronary syndrome, percutaneous coronary intervention (PCI), or valve or coronary bypass grafting surgery within 90 days of procedure
7. Left atrial diameter > 5.0 cm measured within 180 days of procedure (echocardiography or CT)
8. Left ventricular ejection fraction < 35% measured within 180 days of procedure (echocardiography or CT)
9. New York Heart Association (NYHA) class III or IV
10. Previous left atrial surgical or catheter ablation procedure
11. Left atrial surgical procedure or incision with resulting scar (including LAA closure device)
12. Previous tricuspid or mitral valve replacement or repair
13. Heart disease in which corrective surgery is anticipated within 180 days after the procedure
14. Bleeding diathesis or suspected pro-coagulant state
15. Contraindication to long term anti-thromboembolic therapy
16. Presence of any condition that precludes appropriate vascular access
17. Renal failure requiring dialysis
18. Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled with pre-medication

[redacted]

19. Severe pulmonary disease (e.g., restrictive pulmonary disease, constrictive or chronic obstructive pulmonary disease) or any other disease or malfunction of the lungs or respiratory system that produces severe chronic symptoms
20. Women who are pregnant or breastfeeding
21. Presence of other anatomic or comorbid condition that, in the investigator's opinion, could limit the patient's ability to participate in the clinical trial or to comply with follow up requirements, or impact the scientific soundness of the clinical trial results
22. Patient is currently participating in another clinical trial or has participated in a clinical trial within 30 days prior to screening that may interfere with this clinical trial
23. Patient is unlikely to survive the protocol follow up period of 12-months after the procedure
24. Body mass index > 40 kg/m^2
25. Presence of other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.
26. Individuals without legal authority
27. Individuals unable to read or write
28. Patients who have had a ventriculotomy or atriotomy within the preceding 4 weeks of procedure,
29. Patients with prosthetic valves,
30. Patients with a myxoma,
31. Patients with an interatrial baffle or patch as the transseptal puncture could persist and produce an iatrogenic atrial shunt
32. Patient unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation
33. Stroke or TIA (transient ischemic attack) within the last 90 days
34. Stent, constriction, or stenosis in a pulmonary vein.
35. Rheumatic heart disease
36. Severe mitral regurgitation (regurgitant volume ≥ 60 mL/beat, regurgitant fraction ≥ 50%, and/or effective regurgitant orifice area ≥ 0.40cm^2).

5.4 Subject Enrollment

A patient is considered enrolled in the clinical investigation from the moment the patient provides written informed consent.

If subjects, enrolled into the clinical investigation, had an ablation procedure where the TactiFlex SE was used and are later found to have met at least one exclusion criterion or not all inclusion criteria after the ablation procedure, these subjects will continue follow-up in the clinical investigation and will be included in the analysis population. A protocol deviation must be completed on the applicable CRF. Such subjects identified prior to the index procedure should be identified as screen failures and a protocol deviation is not necessary.

5.4.1 Enrollment of Medicare Beneficiaries

This clinical investigation will enroll Medicare beneficiaries that qualify based on the inclusion and exclusion criteria defined for this trial. This IDE clinical trial conforms to all standards of Medicare coverage requirements. The Risks and Benefits section (**Section 15.0**) describes how all enrolled subjects, including Medicare beneficiaries, may be affected by the device under investigation.

[redacted]

The intended clinical benefit of the TactiFlex™ Ablation Catheter, Sensor-Enabled™ is to provide relief of drug-refractory recurrent symptomatic paroxysmal atrial fibrillation. Medicare beneficiaries are expected to experience similar clinical benefit and outcomes from commercially available ablation products. Drug-refractory symptomatic paroxysmal AF impacts 9% of the population of those aged > 65 years and with the aging of the U.S. population, this number is expected to increase. Medicare beneficiaries would benefit from participation in this study because AF increases their risk of stroke and this condition contributes to significant hospitalizations each year as well as death if left untreated. This study would enhance our existing knowledge of clinical solutions for catheter ablations in evaluating the safety and efficacy of the TactiFlex and congruence with the currently accepted medical guidelines for AF treatment.

Subjects enrolled in the clinical investigation are expected to be consistent with the Medicare population based on age and as such, the clinical investigation results are expected to be generalizable to the Medicare population.

5.4.2 Historically Under-Represented Demographic Subgroups

The Sponsor intends to implement FDA's guidance on sex-specific data in medical device clinical investigations to ensure adequate representation of women and other traditionally under-represented demographic subgroups in this clinical investigation. As noted in the guidance, some barriers to participation of women and ethnic minorities in clinical investigations have traditionally been:

- Lack of understanding about main obstacles to participation of such subgroups in clinical research
- Inclusion/exclusion criteria potentially not needed to define the clinical investigation population may unintentionally exclude specific subgroups
- Under diagnosis of disease etiologies and pathophysiology leading to under referral of demographic subgroups
- Avoidance of specific subgroups by investigators and Sponsors due to the perception that it takes more time and resources to recruit them
- Fear of fetal consequences (for female participants)
- Family responsibilities limiting women's ability to commit time for follow-up requirements

The Sponsor will take the following steps to ensure adequate representation of women and racial or ethnic minorities in this clinical investigation:

- Abbott will provide training to investigational site personnel to ensure adequate representation of these demographic subgroups
- Abbott will approach sites without bias or consideration for specific demographic subgroups
- Abbott will have informed consent materials in alternative languages and will work with sites and IRBs/ECs on recruitment materials

5.5 Subject Withdrawal

Each enrolled subject shall remain in the clinical investigation until completion of the required follow-up period; however, a subject's participation in any clinical investigation is voluntary and the subject has the

[redacted]

right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death
- Subject voluntary withdrawal
- Subject lost-to follow-up as described below
- Subject fails to meet all Eligibility Criteria (**Section 5.3**)
- Procedure is aborted prior to (ablation) catheter insertion
- Procedure is aborted prior to RF energy delivery
- Subject's follow-up is terminated according to **Sections 6.6.1-6.6.2**.

The Sponsor must be notified of the reason(s) for subject discontinuation. The site will provide this information to the Sponsor. Investigators must also report this to their respective IRB/EC as defined by their institution's procedure(s).

No additional follow–up will be required or data recorded from subjects once withdrawn from the clinical investigation, except for the status (deceased/alive).

In case of subject withdrawal of consent, the site should make attempts to schedule the subject for a final clinical investigation visit. At this final follow-up visit, the subject will undergo the assessments as outlined for an unscheduled visit in **Section 6.6.5** if the visit does not coincide with a scheduled follow-up visit.

Withdrawn subjects count towards the total enrollment at the site and will not be replaced by enrolling additional subjects.

5.5.1 Lost-to-Follow-up

If the subject misses two consecutive scheduled follow-up time points and the attempts at contacting the subject detailed below are unsuccessful, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following for each time an attempt was made to contact the subject:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, a letter (certified if applicable) should be sent to the subject.
- If a subject misses one or more non-consecutive follow-up contact time points, it will be considered a missed visit. The subject may then return for subsequent visits.
- If the subject misses two consecutive time points and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with General Practitioner, non-clinical investigation cardiologist or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as subject contact.

[redacted]

5.6 Number of Subjects

Three hundred fifty-five (355) subjects will be enrolled in this study and up to 40 sites may participate worldwide. Three hundred five (305) subjects will be enrolled in the main study of this clinical investigation to analyze the primary endpoints. No site may enroll more than 20% (61/305) of the subjects in the main study without Sponsor pre-approval and at least 50% (153/305) of the enrolled main study subjects must be from the United States.

Fifty (50) subjects will be enrolled in the HSP substudy. No site may enroll more than 10 (20%) of the subjects in the HSP substudy without Sponsor pre-approval and at least 25 (50%) of the enrolled HSP substudy subjects must be from the United States.

5.7 Total Expected Duration of the Clinical Investigation

[redacted]The expected duration of each subject's participation is approximately 12 months, from the time of providing informed consent to the completion of the 12-month follow-up visit. Subjects will be exited from the trial at the conclusion of their 12-month follow-up visit. [redacted]The study will be completed after all enrolled subjects either complete the 12-month follow-up visit or are withdrawn from the study.

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

The Principal Investigator is responsible for ensuring all clinical investigation data is collected as outlined in this CIP. However, other site personnel may obtain data to be used in the trial. Physical exams and adverse event assessment may be performed by an investigator, physician, or mid-level provider (i.e. nurse practitioners, physician assistants, or fellows). The neurological assessment needs to be performed by a qualified physician and the NIH Stroke Scale must be administered by a certified assessor.

6.1 Baseline Clinical Assessments

The assessments listed below will be collected from each subject at the Baseline Visit. Information gathered at this visit will be used to verify eligibility of the subject for the trial.

- Documentation of the informed consent process as defined in **Section 5.2.2**
- Demographics
- Medical history, including cardiac arrhythmia history and documentation for the diagnosis of paroxysmal AF
- AAD history, including maximum ineffective dosages and dosages not tolerated
- Anticoagulation drug usage
- Complete physical exam, 12-lead ECG, NYHA assessment, and CHA2DS2VASc score assessment
- NOTE: If these assessments were performed as part of standard of care prior to consent, they may be used if they were completed within 30-days of the initial ablation procedure.

[redacted]

- Neurological assessment by a qualified physician and administration of the NIH Stroke Scale (NIHSS) by a certified assessor must be performed within 14-days of the ablation procedure.
- NOTE: Subjects with new findings on the neurologic assessment/NIHSS are required to have a formal neurological consult and follow-up diffusion-weighted magnetic resonance imaging (MRI) of the brain. If contra-indicated for MRI, then an alternate form of imaging may be performed.
- LVEF and LAD assessment
- NOTE: Echocardiography or CT results obtained within 180 days of the initial ablation procedure may be used to meet eligibility criteria and documented at baseline, with the exception of thrombus assessment.
- Administration of the AF Effect on Quality of Life Survey (AFEQT) and EuroQol Five Dimensions Questionnaire (EQ-5D-5L) quality of life questionnaires
- Documentation of adverse events and protocol deviations that occur after consent and prior to the procedure

6.2 Peri-procedural Considerations

6.2.1 Anticoagulation

The anticoagulation strategies from the 2017 Expert Consensus Statement on Catheter and Surgical Ablation for AF [17] for pre- and post-ablation are outlined below and are recommended to be followed for management of study subjects. However, **it is strongly recommended that a strategy of uninterrupted anti-coagulation be in place for peri-operative management**. All start and stop times of anticoagulants must be documented for the trial. Subjects who are taking coumadin or warfarin will have international normalized ratio (INR) values documented on the day of the procedure and after the drug is restarted after the ablation procedure.

Pre-ablation

- Patients who are therapeutically anticoagulated with warfarin, dabigatran or rivaroxaban prior to the ablation are recommended to have the ablation procedure performed without interruption of the anticoagulant.
- Patients anticoagulated with a novel oral anticoagulant (NOAC) prior to undergoing an AF ablation procedure may have one to two doses of the NOAC withheld prior to AF ablation with re-initiation of the NOAC post-ablation.
- Anticoagulation guidelines that pertain to cardioversion of AF should be adhered to in patients who present for an AF ablation procedure.

Post-ablation

- In patients who are not therapeutically anticoagulated prior to catheter ablation of AF and in whom warfarin will be used for anticoagulation post-ablation, low molecular weight heparin or intravenous heparin should be used as a bridge for initiation of systemic anticoagulation with warfarin following AF ablation.
- Systemic anticoagulation with warfarin or NOAC is recommended for at least 2-months post-ablation of AF. Systemic anticoagulation beyond 2-months post-ablation should be based on the patient's stroke risk profile (not on the perceived success or failure of the ablation procedure).

[redacted]

- In patients who have not been anticoagulated prior to catheter ablation of AF or in whom anticoagulation with a NOAC or warfarin has been interrupted prior to ablation, administration of a NOAC 3 to 5 hours after achievement of hemostasis is reasonable post-ablation.

6.2.2 Antiarrhythmic Drug Therapy

A recommended ablation strategy is provided in **Section 6.3.5**; however, the ablation strategy used for each subject is left to the discretion of the investigator, other than the requirement for PV isolation and the confirmation of entrance block after a minimum 20-minute waiting period. This clinical investigation does not have a requirement that subjects continue/discontinue AADs before the ablation procedure, but AAD usage (start and stop date, time, frequency and dose information) will be documented for the trial prior to and after the subject's procedure(s). If a strategy searching for non-pulmonary vein triggers is employed, it is recommended that that AADs should be discontinued for at least five half-lives and beta-blockers withheld for at least 24-hours prior to the ablation procedure, as per the 2017 Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation [17]. This recommendation does not apply to amiodarone because its half-life is very long [33].

During the blanking period after the ablation procedure, it is recommended that any current AAD medication be continued to aid with healing. Current Class I and III AADs must be withdrawn 4-6 weeks after ablation, unless clinically contraindicated, to assess for recurrence of symptoms and for determination of the need for a repeat ablation during the blanking period. **Sites are to phone subjects 5 weeks after ablation (35 ± 7 days) to remind them to discontinue their AAD medication, unless clinically justified.**

Subjects must be off all Class I and III AADs prescribed for AF/AFL/AT after the blanking period, unless clinically justified. If the investigator determines in their medical judgment that the subject may benefit from a Class I or III AAD during the 9-month evaluation period (post-blanking period), then the investigator should first prescribe a previously ineffective Class I or III AAD up to the historic maximum ineffective dose prior to the ablation procedure. If the historic maximum ineffective dose remains ineffective then a new Class I or III AAD may be initiated.

Subjects using Class I or III AADs without documented AF/AFL/AT recurrence during the follow-up period will not be considered primary effectiveness endpoint failures. However, if the subject requires a new Class I or III AAD or a previously failed Class I or III AAD at a dose greater than the highest ineffective historical dose for AF after the therapy blanking period (≥91 days post-procedure), they will be considered a primary effectiveness endpoint failure.

6.2.3 Pregnancy Testing

A urine pregnancy test shall be performed for women with child-bearing potential with the timing per the site's standard of care after consent and before the study procedure.

6.2.4 Thrombus Assessment

Left atrial thrombus assessment must be performed within one day of the ablation procedure (the day before or the day of the ablation procedure). It is strongly recommended that transesophageal echocardiography (TEE) be used, per the 2017 Expert Consensus Statement [17]. It is recommended that phased-array intracardiac echocardiography (ICE) be used to exclude atrial thrombus only in subjects that cannot undergo TEE (for example, they have an esophageal obstruction or do not have an esophagus) at the time of the procedure.

[redacted]

If a thrombus is discovered within a day or at the day of the procedure, the procedure should be postponed and the subject placed on anticoagulation until the thrombus is resolved and confirmed by imaging. Alternatively, the subject may be withdrawn from the study.

The subject will not need to be re-consented for the trial after the thrombus resolves, provided that the subject continues to meet all eligibility criteria and will undergo an ablation procedure within 90-days of the original consent date unless otherwise indicated by the governing IRB/EC. Once confirmation is obtained demonstrating resolution of the thrombus, the neurological assessment and NIH Stroke Scale must be repeated within 2-weeks of the newly scheduled procedure and these assessments must be used to determine if the subject still meets eligibility for inclusion in the trial.

If the investigator determines after 90 days the thrombus has not resolved, or if the subject no longer meets any of the other eligibility criteria, the subject will be identified as a screen failure and the screening log should be updated.

6.3 Ablation Procedure

6.3.1 Confirmation of Subject Eligibility

Any subject who does not meet eligibility requirements will be a screen failure and will be excluded from this trial and will not have the TactiFlex SE catheter inserted into their vasculature.

- Neurological assessment and administration of the NIHSS by a certified assessor must be performed within 14-days of the ablation procedure.
- Thrombus assessment must be performed as outlined in **Section 6.2.4** prior to ablating the subject.
- Pregnancy test must be performed as per **Section 6.2.3**, if applicable.

6.3.2 Procedure Timing

For those subjects meeting eligibility criteria and who are enrolled in the trial, it is recommended that the initial ablation procedure be performed within 14 days of consent because the neurological assessment and NIH Stroke Scale must be performed within 2-weeks of the ablation procedure and these assessments are used to determine if the subject meets eligibility for inclusion in the trial. It is required that the initial ablation procedure is performed within 30 days of consent unless a thrombus is identified within a day of a scheduled procedure as per **Section 6.2.4**. Subjects that fail the thrombus assessment and meet all other screening criteria may have the initial investigational procedure postponed up to 90 days after their consent date while the thrombus is given a chance to resolve. If the investigator determines after 90 days the thrombus has not resolved, the subject will be identified as a screen failure.

6.3.3 General Considerations

- Physicians performing ablations must be qualified operators and trained on the study. Each physician who ablates during a particular case needs to be documented on the Procedure CRF. Fellows will not be allowed to perform ablations unless an exception is made by Abbott's Medical Director in writing prior to the fellow performing ablations for this trial. Any fellows granted an

[redacted]

exception must be trained per the study-specific Training Plan and on the Delegation of Authority Log.

- The subject's rhythm when they enter the EP lab will be documented for the trial.
- All cardioversions that occur from the time the subject enters the lab to the start of the procedure and during the procedure will be documented.
- Details of the ablation procedure will be recorded on the appropriate CRF(s)
- It is strongly recommended that vascular access be obtained using ultrasound to minimize complications.
- It is recommended that heparin be administered prior to trans-septal puncture during the AF catheter ablation procedure and adjusted to achieve and maintain an ACT of at least 300 seconds.
    - Administration of protamine to reverse heparin is acceptable.
- Use of an ICE probe during the procedure to guide septal puncture and to monitor catheter position and manipulation is strongly recommended.
- It is strongly recommended that esophageal temperature be monitored using an esophageal temperature probe at the anatomical location nearest the site of energy delivery. Alternatively, esophageal deviation may be performed when ablating near the esophagus.
    - Termination of energy is strongly recommended if a >1°C rise in esophageal temperature is observed.
- The AutoMark feature of the EnSite™ Cardiac Mapping system must be running during the ablation procedure.
    - It is recommended that the default AutoMark Placement Settings are used (Away time, Min AutoMark Time, AutoMark Spacing). For more information, see the EnSite™ AutoMark Module *Instructions for Use* document.

6.3.4 Ablation Parameters

The procedure should be performed according to the TactiFlex SE investigational *Instructions for Use* document using the recommended ablation parameters as noted in the document.

> **Note:** Investigators treating HSP substudy subjects are required to use ablation power settings of 40-50 Watts in the left atrium, unless medically justified. Investigators not treating HSP substudy Subjects are to follow the ablation power recommendations provided in the investigational *Instructions for Use* document.

6.3.4.1 Contraindications

The TactiFlex SE catheter is contraindicated for:

- Patients who have had a ventriculotomy or atriotomy within the preceding four weeks.
- Patients with prosthetic valves as the catheter may damage the prosthesis.
- Patients with an active systemic infection as this may increase the risk for cardiac infection.
- Use in coronary vasculature due to risk of damage to the coronary arteries.

[redacted]

- Patients with a myxoma or an intracardiac thrombus as the catheter could precipitate an embolus.
- The transseptal approach in a patient with an interatrial baffle or patch because the opening could persist and produce an iatrogenic atrial shunt.
- The retrograde trans-aortic approach in patients who have had aortic valve replacement.
- Patients unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation.

Refer to the the TactiFlex SE investigational Instructions for Use for Warnings and Precautions.

6.3.5 Ablation Strategy

The ablation procedure strategy recommended for this clinical investigation is outlined in **Figure 6**

- Following trans-septal access, a standard treatment scheme for mapping and ablation should be conducted.
- Subjects should first receive ablations to achieve pulmonary vein isolation (PVI), preferably via wide area circumferential ablation (WACA) or individual pulmonary vein isolation.
    - Posterior wall isolation and so-called ablation "lines" (i.e. roof, mitral, anterior) are not part of the recommended ablation strategy for this study.
        - Should investigators choose to perform ablation lines at their discretion, investigators are required to confirm bi-directional block per the Consensus Statement [17].
    - Use of robotic systems or Stereotaxis to assist with the procedure is not allowed.
    - Ablation in the left atrium using an ablation catheter other than TactiFlex SE is not allowed and will result in failing the Primary Effectiveness Endpoint. In addition, any ablations performed in the atria using an ablation catheter other than TacitFlex SE will result in a protocol deviation.
- After completing initial PVI, **a minimum 20-minute wait period is required before confirming electrical isolation of each pulmonary vein via entrance block, at a minimum**. Entrance block can be confirmed by placing a multipolar mapping catheter (i.e. spiral or HD Grid) in the lumen of the pulmonary vein and checking for the presence and location of suspected gaps [20, 34]. If it is not possible for the operator to place a multipolar catheter in the lumen of the pulmonary vein, the TactiFlex SE catheter may be used to confirm entrance block.
- All subjects with a history of typical atrial flutter or induced CTI-dependent atrial flutter need to undergo concomitant AFL ablation and operators are required to verify bi-directional block by mapping and pacing maneuvers after initial bi-directional block is achieved.
    - It is recommended that the ablation of the CTI line be performed during the 20-minute post-PVI waiting period. Alternatively, if preferred by the operator, patients with a history of typical AFL may have their CTI ablated before the starting PVI ablation in the left atrium.
- If the patient is still in AF after first-pass PVI, cardioversion is recommended. Alternatively, suspected gaps and non-PV AF targets may be ablated at the discretion of the investigator. Example Non-PV ablation targets include posterior wall foci and SVC isolation [35, 36].

[redacted]

- If the subject is in sinus rhythm following initial PVI, isoproterenol may be administered to identify gaps in PVI ablation and to identify any additional AF triggers. Non-PV ablation targets may be identified and ablated if AF is re-induced after isoproterenol challenge [37]. Adenosine challenge is not recommended, but permitted if it is part of the operator's standard of care.
- If PV reconnection occurs during or after the 20-minute wait period following initial PV isolation of each vein, the vein(s) that reconnected and whether it was successfully isolated (as confirmed by entrance block) after administration of additional ablation lesions will be documented on the CRF. Another 20-minute waiting period is not required after performing touch-up ablation lesions for reconnected PVs.
- Subjects with a documented history of AT or other SVT or if these arrhythmias are induced at the time of AF ablation (or isoproterenol challenge), may undergo additional targeted ablation as clinically indicated.

6.3.6 End of Procedure Activities

- At the end of the procedure (within 24 hours), verify that the subject has not experienced pericardial effusion by ICE or transthoracic echocardiogram (TTE).
- Any protocol deviations and adverse events must be documented on the appropriate CRF.
- The data from the entire procedure recorded on the investigational EnSite system and the Ampere generator log files should be anonymized and labeled with the study information and Subject ID and sent to Abbott within a reasonable time frame (within 10 days).

[redacted]

[redacted]

Clinical Investigation Plan

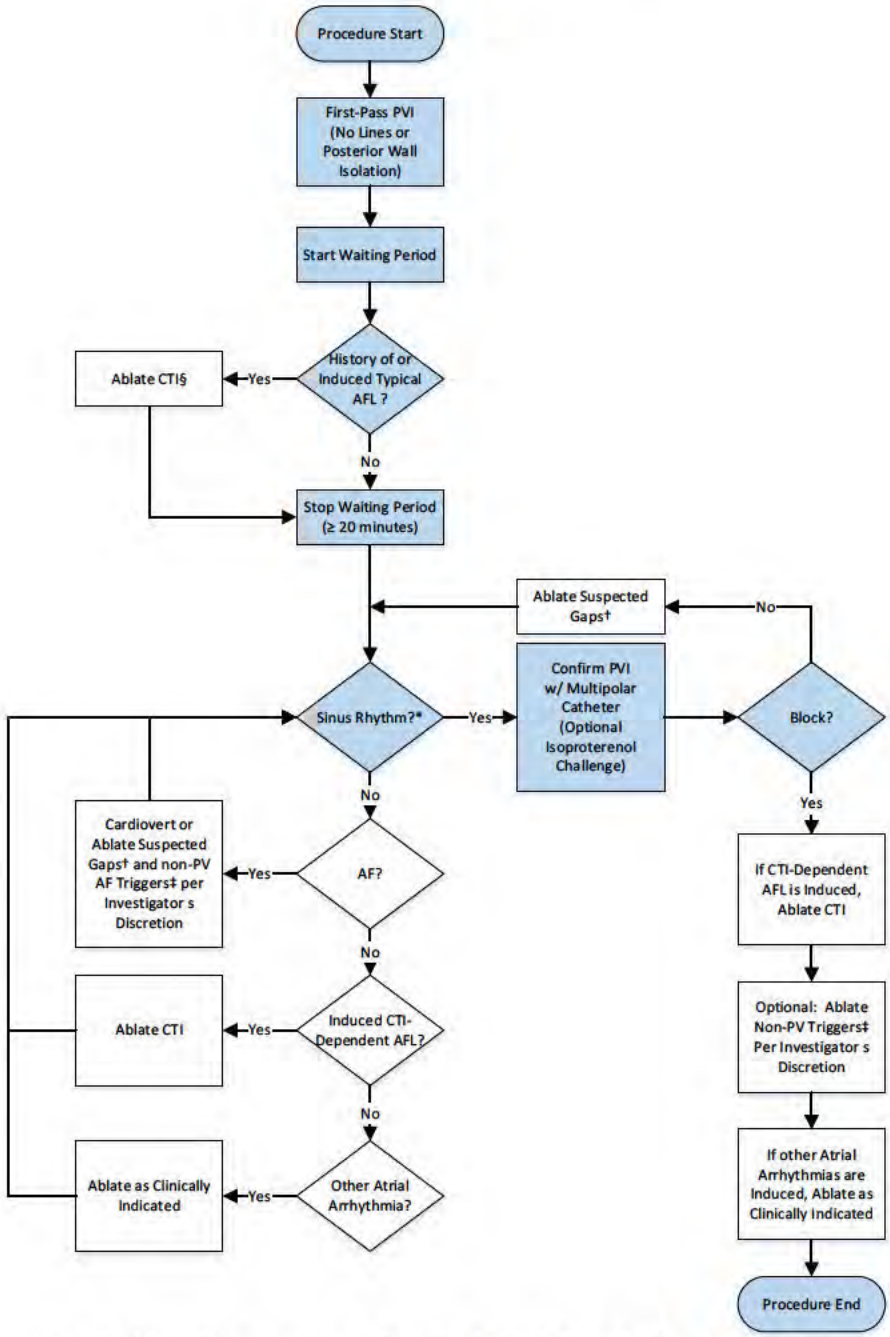

Figure 6. Recommended Ablation Strategy for the TactiFlex PAF study. Only the blue-shaded steps are expected to apply to most subjects. §If a patient has a history of typical AFL, the CTI may also be ablated before starting PVI. *If no gaps or non-PV triggers can be identified, or additional ablation is deemed futile by the investigator, cardiovert, check for PVI isolation, and end the procedure. †For example, the location of a suspected gap may be identified using a multipolar catheter during entrance block confirmation. ‡For example, posterior wall or SVC isolation.

[redacted]

6.3.7 Description of Study Activities Performed by Abbott Field Representatives

Trained Abbott personnel may provide technical expertise and technical guidance on the use of the investigational devices. However, the Principal Investigator remains responsible for ensuring all clinical investigation data is collected as required per the CIP. An Abbott field representative may assist with obtaining procedure data from the EnSite system and Ampere generator for documentation for the trial and/or sending procedure data to Abbott. An Abbott field representative may also run the investigational EnSite software, at the request of the Investigator.

6.4 Pre-Discharge Visit (In-hospital)

Patients may be discharged at the discretion of the investigator after the required testing, listed below, has been performed, which includes a neurologic assessment 12-36 hours after the procedure. This may require the subject to stay in the hospital the night after the procedure. It is strongly recommended that the investigator performing the ablation procedure personally evaluates the subject the evening after the procedure and/or the morning following the procedure and maintains active surveillance of the subject's postoperative care and condition for at least 72-hours or prior to discharge, whichever occurs first.

The following are required testing for the Pre-Discharge Visit:

- Complete physical exam
- 12-lead ECG
- Neurological assessment by a qualified physician and administration of the NIHSS by a certified assessor must be performed ≥12 hours post-procedure prior to discharge, but no later than 36 hours after the procedure.

  NOTE: Subjects with new findings on the neurologic assessment/NIHSS are required to have a formal neurological consult and follow-up diffusion-weighted magnetic resonance imaging (MRI) of the brain. If contra-indicated for MRI, then an alternate form of imaging may be performed.
- Document AAD and anticoagulant drug usage
- Document adverse events and protocol deviations
  - If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.

If the subject requires an extended hospitalization due to a complication or other reason, the neurological exam and NIHSS assessment should be performed within 36-hours of the procedure. All other pre-discharge testing should be performed prior to discharge, but no later than 72 hours post-procedure.

6.5 Blanking Period

A blanking period of 90-days will be employed after the initial ablation procedure and then followed by a 9-month evaluation period for a total of 12-months of follow-up. Early recurrence of AF, AFL, or AT within the blanking period will not be considered treatment failures. During the blanking period, adjustment of antiarrhythmic medications, cardioversions, and one repeat ablation procedure (31-80 days after the initial procedure) may be performed.

[redacted]

6.6 Follow-up Assessments

6.6.1 Follow-Up for Consented Subjects that Fail Screening and/or TactiFlex SE not Inserted

Consented subjects that fail screening criteria and/or never have a TactiFlex SE catheter inserted will be withdrawn from the study. Documentation of any AEs that may have occurred since the subject signed informed consent should be collected on an AE CRF as part of a scheduled or unscheduled visit (**Section 6.6.5**).

6.6.2 Follow-Up for Consented Subjects - TactiFlex SE Inserted, No RF Delivered

If for any reason, a subject has the TactiFlex SE inserted into their vasculature, but no ablation is performed and the subject will not be rescheduled to receive another ablation procedure within 90 days of their consent date, the subject will be followed for 30 days to assess safety and then withdrawn from the trial. Follow-up at 30-days will be conducted via a phone call to the subject (may also be an on-site visit). Documentation of any AEs that may have occurred since the subject signed informed consent should be collected on an AE CRF as part of a scheduled or unscheduled visit (**Section 6.6.5**).

6.6.3 Follow-Up for All Subjects with TactiFlex SE Inserted and RF Delivered

Each enrolled subject that has had the TactiFlex SE catheter inserted into their vasculature and received RF energy delivery will undergo the following follow-up procedures described below from 7 days through 12 months post-ablation.

7-Day (7 ± 2 days) Follow-up Visit

This visit constitutes a phone call to the subject (but may also be performed in-person) after each ablation procedure (initial and if applicable, a repeat procedure) and requires documentation of the following:

- Document AAD and anticoagulant drug usage
- Document adverse events and protocol deviations
    - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), have the subject schedule a visit with the investigator to determine if CT or MRI imaging of the pulmonary veins should be performed.
    - If the subject describes symptoms suggestive of atrio-esophageal fistula such as chest pain, painful swallowing, fever, and/or describes symptoms of stroke, have the subject schedule a visit with the investigator immediately or go to the emergency room based on the severity of the symptoms.
    - If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.

5-Week (35 ± 7 days) Phone Call

Sites are to phone subjects 5 weeks after ablation (35 ± 7 days) to remind them to discontinue their AAD medication, unless a clinical justification can be provided for keeping the subject on AADs for a period longer than 42 days after the ablation procedure.

[redacted]

- Document AAD and anticoagulant usage
- Document adverse events and protocol deviations
    - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), have the subject schedule a visit with the investigator to determine if CT or MRI imaging of the pulmonary veins should be performed.
    - If the subject describes symptoms suggestive of atrio-esophageal fistula such as chest pain, painful swallowing, fever, and/or describes symptoms of stroke, have the subject schedule a visit with the investigator immediately or go to the emergency room based on the severity of the symptoms.
    - If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.

3-Month (91 + 14 days) Follow-Up Visit

The 3-month follow-up visit is a scheduled in-person site visit.

- 12-lead ECG
- Document AAD and anticoagulant usage
- Administer the AFEQT and EQ-5D-5L questionnaires
- Document adverse events and protocol deviations
    - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), complete CT or MRI imaging of pulmonary veins.
    - If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.
- Provide the subject with a TTM device (regardless of having an implantable device capable of recording ECGs such as an ICM/ILR, pacemaker, or ICD) for scheduled heart rhythm transmissions and transmission of symptomatic episodes.
    - The first scheduled TTM transmission is to be within the 14-day period following the 3-month visit (1-14 days after the visit). At least one TTM transmission must occur in every 14-day peri od between the 3-month and 12-month follow-up visits (1-14,15-28, 29-42, 43-56, etc. days after the 3-month visit). As permitted by local regulations, it is recommended that either the core lab or site personnel contact the subjects to help them perform each scheduled TTM transmission and verify that the transmission has been received by the core lab.

6-Month (181 ± 21 days) Follow-Up Visit

The 6-month follow-up visit is a phone call to the subject but may also be performed in-person.

- Document AAD and anticoagulant usage
- Administer the AFEQT and EQ-5D-5L questionnaires

[redacted]

- Document adverse events and protocol deviations
    - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), have the subject schedule a visit with the investigator to determine if CT or MRI imaging of the pulmonary veins should be performed.
    - If the subject describes symptoms suggestive of atrio-esophageal fistula such as chest pain, painful swallowing, fever, and/or describes symptoms of stroke, have the subject schedule a visit with the investigator immediately or go to the emergency room based on the severity of the symptoms.
    - If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.
- Continue with TTM monitoring for scheduled heart rhythm transmissions and transmission of symptomatic episodes.
    - The first scheduled TTM transmission is to be within the 14-day period following the 3-month visit (1-14 days after the visit). At least one TTM transmission must occur in every 14-day period between the 3-month and 12-month follow-up visits (1-14,15-28, 29-42, 43-56, etc. days after the 3-month visit). As permitted by local regulations, it is recommended that either the core lab or site personnel contact the subjects to help them perform each scheduled TTM transmission and verify that the transmission has been received by the core lab.

12-Month (365 ± 30 days) Follow-Up Visit

The 12-month follow-up visit is a scheduled in-person site visit.

- 12-lead ECG
- Document AAD and anticoagulant usage
- Administer the AFEQT and EQ-5D-5L questionnaires
- Document adverse events and protocol deviations
    - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), complete CT or MRI imaging of pulmonary veins.
- Administer a 24-hour Holter monitor
- Collect the TTM monitor from the subject

6.6.4 Repeat Ablation Procedures

One ablation procedure is allowed during the blanking period (between 31 and 80 days post-initial procedure) due to AF/AFL/AT recurrence without being considered an effectiveness endpoint failure. The repeat procedure must be performed with the TactiFlex SE catheter using the recommended parameters listed in the *Instructions for Use* document and in **Section 6.3**. The TactiFlex SE catheter cannot be used for repeat procedures that occur ≥81 days after the initial procedure or if the subject requires a third ablation procedure at any time during the follow-up period (a marketed ablation catheter should be used).

[redacted]

The following assessments need to be performed if a repeat ablation is required.

- Neurological assessment and administration of the NIHSS by a certified assessor must be performed within 14-days of the repeat ablation procedure.
- Thrombus assessment must be performed as outlined in **Section 6.2.4** prior to ablating the subject.
- Pregnancy test must be performed as per **Section 6.2.3**, if applicable.
- Verification of the exclusion of pericardial effusion by ICE or TTE must also be performed prior to the conclusion of the procedure.
- Document adverse events and protocol deviations

A 7-day (± 2 days) follow-up phone call to the subject will need to be conducted after the repeat procedure. All other follow-up visits will occur as previously scheduled from the initial ablation procedure. Note that the 90-day blanking period is still in place from the initial procedure.

If the subject requires a repeat procedure for AF/AFL/AT recurrence >80 days after the initial ablation procedure, or the subject requires a third ablation procedure, then the subject will be considered an effectiveness endpoint failure regardless of documentation of a >30 second AF/AFL/AT episode.

The data from the entire procedure recorded on the investigational EnSite system should be anonymized and labeled with the study information and Subject ID and sent to Abbott within a reasonable time frame (within 10 days).

6.6.5 Unscheduled Visits

If a subject is seen by a healthcare provider from their study site for any reason outside of a regularly scheduled study visit, or if the subject is being withdrawn from this clinical investigation for any reason and the final follow-up is being conducted outside of a regularly scheduled visit, the following information should be documented, as applicable.

- 12-lead ECG
- Document AAD and anticoagulant usage
- Document adverse events and protocol deviations
    - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), have the subject schedule a visit with the investigator to determine if CT or MRI imaging of the pulmonary veins should be performed.
    - If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.
- If the subject is withdrawing from the study, complete the Study Completion CRF.

Unscheduled Visits for the purpose of subject withdrawal from the clinical investigation may be performed by telephone or in-person at the study site.

[redacted]

6.6.6 Patient Reported Outcome Measures – AEFQT and EQ-5D-5L Questionnaires

Designated site personnel will administer patient-reported outcome questionnaires. It is important the subject understands the meaning of all words and instructions in the questionnaires. The subject should be instructed to ask any questions about the questionnaires if further explanation is needed. Once the questionnaires are completed, the site personnel will review them for completeness to verify that all questions have been answered according to the directions provided.

The following patient-reported outcome measures will be collected:

- AF Effect on Quality of Life Survey (AFEQT)
- EuroQol Five Dimensions Questionnaire (EQ-5D-5L)

The AFEQT questionnaire is an AF-specific health-related quality of life questionnaire designed to be used in different clinical settings including clinical research, survey studies, or clinical practice to assess the impact of AF on a patient's quality of life and possibly to assess changes with treatment. The AFEQT is a self-administered questionnaire that should take approximately 5-minutes to complete and consists of 20 questions. Four of the 20 questions target AF-related symptoms, 8 questions evaluate daily function, and 6 questions assess AF treatment concerns on a 7-point Likert scale (1= "Not at all…" to 7 "Extremely…"). Two of the questions are not scored and are to assess the subject's satisfaction with treatment. The AFEQT questionnaire should ideally be administered prior to the subject being seen by the physician to ensure the subject's responses are not influenced by the physician's evaluation. If other questionnaires are to be administered at the same time, the AFEQT should be completed first so that answers to other questionnaires do not influence the response to the AFEQT.

The EQ-5D-5L questionnaire is a standardized measure of health status that is applicable to a wide range of health conditions and treatments. It provides a simple descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health as well as in population health surveys. EQ-5D-5L is designed for self-completion and is ideally suited for use in postal surveys, in clinics, and in face-to-face interviews and takes only a few minutes to complete. The questionnaire includes five dimensions assessing mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is measured based on responses to 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. Respondents evaluate their overall health status using a visual analogue scale, which can easily be converted to quality-adjusted life years for cost utility analysis.

Note that it will not be a deviation for the 6-month visit administered by phone to not have the visual analogue scale of the EQ-5D-5L questionnaire completed. Research personnel should use the EQ-5D-5L Script for Telephone Interview questionnaire for visits conducted over the phone.

6.6.7 Schedule of Events

The schedule of activities specific to this clinical investigation are described in the preceding sections and are summarized in **Table 4**.

[redacted]

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Table 4. Schedule of Events for TactiFlex PAF

Activity	Enrollment/ Baseline	Procedure (≤14-days of consent[1,2])	Pre-Discharge (Post-Procedure Before discharge and ≤72 hrs)	7-Day Phone Call[3] (7± 2 days)	5-Week Phone Call (35 ± 7 days)	3-Month In-Person (91+14 days)	6-Month Phone Call[3] (181 ± 21 days)	12-Month In-Person (365 ± 30 days)	Un-scheduled Visit (Phone or In-Person)
Informed Consent	X								
Verification of Eligibility	X	X[4,5]							
Demographics	X								
Medical History[6]	X								
LVEF and LAD	(X)[7]								
Physical Examination	X		X						
CHA_2DS_2VASc	X								
Neurological Assessment & NIHSS	X		X (12-36 hours post-procedure)[8]						
Diffusion-weighted MRI - Brain	(X)[9]		(X)[9]						
NYHA	X								
AAD & Anticoagulant Medications	X		X	X	X	X	X	X	X
12-Lead ECG	X		X			X		X	X
AFEQT & EQ-5D-5L Questionnaires	X					X	X	X	
24-Hour Holter								X	
Urine Pregnancy Test		(X)[5]							
Confirm absence of thrombus		X[4]							
Ablation procedure		X							
EnSite Case File & Ampere Log File Anonymization and Collection		X							
Reminder to Discontinue AAD use					X[10]				
Confirm absence of pericardial effusion or cardic tamponade (TTE or ICE)		X[11]	(X)[12]	(X)[12]	(X)[12]	(X)[12]	(X)[12]		(X)[12]
Trans-Telephonic Monitoring (TTM)						X[13]	X[13]	X[13]	

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Activity	Enrollment/ Baseline	Procedure (≤14-days of consent[1,2])	Pre-Discharge (Post-Procedure Before discharge and ≤72 hrs)	7-Day Phone Call[3] (7± 2 days)	5-Week Phone Call (35 ± 7 days)	3-Month In-Person (91+14 days)	6-Month Phone Call[3] (181 ± 21 days)	12-Month In-Person (365 ± 30 days)	Un-scheduled Visit (Phone or In-Person)
CT or MRI of pulmonary veins				(X)	(X)	(X)	(X)	(X)	(X)
Adverse Event Assessment	(X)	X	X	X	X	X	X	X	X
Document Deviations	X	X	X	X	X	X	X	X	X
Study Completion (Withdrawal)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)

(X) If applicable

1. For those subjects meeting eligibility criteria and are enrolled in the trial, it is recommended that the ablation procedure be performed within 14 days of consent because the neurological assessment and NIH Stroke Scale must be performed within 2-weeks of the ablation procedure and these assessments are used to determine if the subject meets eligibility for inclusion in the trial. It is required that the ablation procedure is performed within 30 days of consent unless a thrombus is identified within a day of a scheduled procedure as per **Section 6.2.4**. Subjects that fail the thrombus assessment and meet all other screening criteria may have the investigational procedure postponed up to 90 days after their consent date while the thrombus is given a chance to resolve.
2. Repeat ablation procedures conducted 31-80 days of the initial procedure with the TactiFlex SE catheter should re-collect the same information as the initial procedure.
3. The 7-day and 6-month visits will be conducted a phone call. However, these visits may be conducted in-person.
4. Left atrial thrombus assessment must be performed within one day of the ablation procedure (the day before or the day of the ablation procedure). It is strongly recommended that TEE be used. It is recommended that ICE be used to exclude atrial thrombus only in subjects that cannot undergo TEE at the time of the procedure.
5. A urine pregnancy test shall be performed for women with child-bearing potential with the timing per the site's standard of care after consent and before the study procedure.
6. Medical history includes cardiac arrhythmia history and documentation for the diagnosis of paroxysmal AF.
7. Echocardiography or CT results obtained within 6-months of the initial ablation procedure may be used to meet eligibility criteria and documented at baseline, with the exception of thrombus assessment.
8. The neurological exam and NIHSS must be performed ≥12 hours, but no later than 36 hours after the procedure.
9. Subjects with new findings on the neurologic assessment are required to have a formal neurological consult and follow-up diffusion-weighted magnetic resonance imaging (MRI) of the brain. If the subject is contra-indicated for MRI, then an alternate form of imaging may be used.
10. Patients receive a phone call to be remined to discontinue their AAD usage unless clinical justification can be provided.
11. TTE or ICE imaging must be performed prior to the conclusion of the procedure to exclude pericardial effusion.
12. If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.
13. TTMs are collected every 2 weeks and whenever the subject is experiencing a symptomatic episode starting at 3-months post-procedure to 12-months. At least one TTM transmission must occur in every 14-day period between the 3-month and 12-month follow-up visits (1-14,15-28, 29-42, 43-56, etc. days after the 3-month visit). As permitted by local regulations, it is recommended that either the core lab or site personnel contact the subjects to help them perform each scheduled TTM transmission and verify that the transmission has been received by the core lab.

6.7 Core Laboratory

A core lab will be used for the collection, interpretation, and collation of data collected from the following sources:

- TTM
- 24-hour Holter monitoring
- 12-lead ECGs

The core lab will provide independent review of this data by appropriately trained personnel using standardized procedures to interpret TTM, 24-hour Holter, and 12-lead ECG tracings for adjudication of atrial arrhythmias. Findings will be communicated to the investigator and to Abbott. The core lab's adjudication findings will be used for analysis of effectiveness outcomes.

7.0 ADVERSE EVENTS

To comply with worldwide standards and guidelines on clinical investigation adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

7.1 Definition

7.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device under investigation.

7.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death,

b) Led to a serious deterioration in health of the subject, that either resulted in

   1. a life-threatening illness or injury, or
   2. a permanent impairment of a body structure or a body function, or
   3. in-patient hospitalization or prolongation of existing hospitalization, or
   4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
   5. chronic disease

c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be an SAE.

7.1.3 Device Deficiency/Device Malfunction

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

7.2 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an AE is to be **determined by the Investigator** and recorded on the appropriate CRF form. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

7.2.1 Adverse Device Effect (ADE)

The following definition will be used to categorize non-serious procedure or device-related AEs:

- An adverse event related to the use of an investigational medical device.
- This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
- This definition includes any event resulting from the use error or from intentional misuse of the investigational medical device.

7.2.2 Serious Adverse Device Effect (SADE)

The following definition will be used to categorize serious procedure or device-related AEs:

- Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
- This definition includes events related to the investigational medical device.

7.2.3 Unanticipated Serious Adverse Device Effect (USADE)

A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

7.2.4 Unanticipated Adverse Device Effect (UADE)

Unanticipated adverse device effect (UADE) refers to any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan

or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.3 Adverse Event and Device Deficiency/Device Malfunction Reporting

7.3.1 Adverse Event Reporting

General AE Reporting

Safety surveillance and reporting starts as soon as the patient is enrolled in the clinical investigation. Adverse event data, including deaths, will be collected starting at the time of enrollment (after consent) and throughout the 12-month follow-up period and will be reported to the Sponsor on the Adverse Event CRF. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical investigation or the subject withdraws from the clinical investigation.

All adverse events regardless of severity and relationship to the study device(s) or the study procedure should be submitted; exceptions listed below.

Recurrence of AF, AFL, or AT are not considered reportable adverse events unless they occur in severity, frequency, or other manner that is significantly worse than the subject's baseline condition. Recurrence of AF, AFL, or AT should be reported on an appropriate Follow-Up Visit CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported. A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered and SAE.

An offline form will be made available to allow the investigator to report AEs in the event the entry cannot be made in the EDC. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

SAE Reporting

The investigator should report all SAEs to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines
All Sites	SAEs must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The date the site staff became aware the event met the criteria of an SAE must be recorded in the source document. The Investigator will further report the SAE to the local IRB/EC according to the institution's IRB/EC reporting requirements.

7.3.2 Unanticipated (Serious) Adverse Device Effect Reporting to Sponsor and IRB/EC

The Sponsor requires the Investigator to report any USADE or UADE to the Sponsor within 3 calendar days of the investigator's knowledge of the event, unless local requirements are more stringent, and to the IRB/EC per IRB/EC requirements.

7.3.3 Device Deficiency/Malfunction Reporting

All device deficiencies/malfunctions should be reported on the appropriate CRF form.

The investigator should report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than outlined below.

Clinical Sites	Reporting timelines
All Sites	Device deficiencies/malfunctions must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The device should be returned to the Sponsor.

Device deficiencies/malfunctions should be reported to the IRB/EC per the investigative site's local requirements.

An offline form will be made available to allow the investigator to report device deficiencies/malfunctions in the event that the entry cannot be made in the EDC system. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

7.3.4 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs and reportable device deficiencies/malfunctions to the country regulatory authority, per local requirements.

Note: Reportable device deficiencies/malfunctions include device deficiencies/malfunctions that might have led to an SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

Clinical investigation SAEs and device deficiencies/malfunctions reportable per MedDEV 2.7/3 regulations will be submitted to European Competent Authorities by the Sponsor's Clinical Safety Group. Contact details are provided in **Appendix VIII**.

For investigational sites in Germany, Sites and Sponsor will follow the reporting obligations provided in **Appendix XI**.

8.0 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical investigation. Additional details on statistical analyses, including justification of clinical investigation design, sensitivity analyses, poolability analyses, subgroup analyses and analysis of descriptive endpoints, may be maintained in a separate Statistical Analysis Plan (SAP).

8.1 Analysis Populations

[redacted]

[redacted]

8.1.1 Full Analysis Set (FAS)

[redacted]

8.1.2 Per Treatment Evaluable (PTE) Analysis Population

[redacted]

8.1.3 Primary Safety Analysis Population

[redacted]

8.1.4 Primary Effectiveness Analysis Population

[redacted]

8.2 Statistical Analyses

8.2.1 Primary Endpoint Analyses

8.2.1.1 Primary Safety Endpoint Analysis

[redacted]

8.2.1.2 Primary Effectiveness Endpoint Analysis

[redacted]

8.2.2 Secondary Endpoint Analyses

8.2.2.1 AAD-Free Secondary Effectiveness Endpoint

[redacted]

8.2.2.2 Single-Procedure Secondary Effectiveness Endpoint

[redacted]

[redacted]

8.2.2.3 Symptomatic Secondary Effectiveness Endpoint

[redacted]

8.2.3 Additional Data

The additional data listed in **Section 4.4** will be reported using only summary statistics and no hypothesis tests with pre-specified criteria will be performed. These descriptive endpoints will be reported separately for Main Study subjects and HSP Substudy subjects. An as treated analysis will be conducted using the Additional Data as described in the SAP.

[redacted]

8.3 Sample Size Calculation and Assumptions

[redacted]

8.3.1 Sample Size for Primary Safety Endpoint

[redacted]

[redacted]

8.3.2 Sample Size for Primary Effectiveness Endpoint

[redacted]

8.3.3 Sample Size for AAD-Free Secondary Effectiveness Endpoint

[redacted]

8.3.4 Sample Size for Single-Procedure Secondary Effectiveness Endpoint

[redacted]

8.3.5 Sample Size for Symptomatic Secondary Effectiveness Endpoint

[redacted]

8.4 Timing of Analysis

The primary endpoint analysis will be performed and the pre-market approval (PMA) clinical report will be submitted after the all subjects have exited the clinical investigation.

8.5 Subgroup Analysis

Subgroup analyses will be performed and will be outlined in the Statistical Analysis Plan (SAP).

8.6 Multiplicity

No adjustments for multiplicity will be made for analysis of the primary safety and effectiveness endpoints.

Analysis of the secondary endpoints will be controlled to prevent inflation of Type I error using an appropriate statistical methodology as detailed in the Statistical Analysis Plan (SAP).

[redacted]

Clinical Investigation Plan

8.7 Pooling Strategy

Pooling will be performed and will be outlined in the Statistical Analysis Plan (SAP).

8.8 Procedures for Accounting for Missing Data

All analyses will be based on available data with missing data excluded unless otherwise specified in the analysis population for each endpoint. In order to assess the impact of missing data on the primary safety endpoint and primary effectiveness endpoint results, a sensitivity analysis will be performed as detailed in the SAP.

8.9 Planned Interim Analysis

No interim analyses involving the testing of primary safety or primary effectiveness endpoint hypotheses are planned for this study.

8.10 Statistical Criteria for Termination

The independent DSMB may elect to implement stopping rule(s) for the study that are based statistical criteria that will be documented in the DSMB charter document.

8.11 Success Criteria

The trial will be considered successful if the null hypotheses for both the primary safety and effectiveness endpoints are rejected.

8.12 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical plan. Less significant changes to the planned analyses will be documented in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator/institution will permit direct access to source data/documents for the purpose of performing clinical investigation-related monitoring, audits, IRB/EC review and regulatory inspections.

Subjects providing informed consent are agreeing to allow clinical investigation monitors or regulatory authorities including foreign countries to review, in confidence, any records identifying the subjects in this clinical investigation. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the subject's personal and private information.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical investigation. Sites will be selected based upon review of a recent site assessment, if applicable, and the qualifications of the investigators who will participate in the clinical investigation.

10.2 Clinical Investigation Finances and Agreements

The clinical investigation will be financed by Abbott. Investigational sites will be compensated by Abbott for participation in the clinical investigation per the conditions of agreement between the Sponsor and the Investigational site.

10.3 CIP Amendments

Approved CIP amendments will be provided to the Investigators by the Sponsor prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB/EC or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB's/EC's approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

Acknowledgement/approval by the IRB/EC of the CIP amendment must be documented in writing prior to implementation of the CIP amendment. Copies of this documentation must also be provided to the Sponsor.

10.4 Training

10.4.1 Site Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical investigation personnel will include, but is not limited to, the CIP requirements, investigational device usage, electronic case report form completion and clinical investigation personnel responsibilities. All Investigators and clinical investigation personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigators and clinical investigation personnel must not perform any CIP-related activities that are not considered standard of care at the site.

10.4.2 Training Required for the Use of the Device

All investigators involved in the conduct of this clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately. Proof of training will be documented and stored in the appropriate archiving system

10.5 Monitoring

Sponsor and/or designee will monitor the clinical investigation over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the clinical investigation according to the CIP and applicable regulations and has signed the Investigator Agreement (for US) or the Clinical Trial Agreement (for OUS).

- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical investigation and should have access to an adequate number of appropriate subjects to conduct the clinical investigation.
- Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to CIP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records. A monitoring visit sign-in log will be maintained at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical investigation-related documents.

10.6 Deviations from CIP

The Investigator should not deviate from the CIP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing.

No waivers for CIP deviations will be granted by the Sponsor. All deviations must be reported to the Sponsor using the Deviation CRF. The occurrence of CIP deviations will be monitored by the Sponsor for evaluation of investigator compliance to the CIP and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB/EC or equivalent committee of all CIP deviations in accordance with their specific IRB/EC or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CIP or any other conditions of the clinical investigation may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, Sponsor may terminate the investigator's participation in the clinical investigation.

10.7 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical investigation records, including source documentation, for inspection during a Quality Assurance audit.

In the event that an investigator is contacted by a Regulatory Agency in relation to this clinical investigation, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide Sponsor with copies of all correspondence that may affect the review of the current clinical investigation (e.g., Form FDA 483, Inspectional Observations, Warning

Letters, Inspection Reports, etc.). Sponsor may provide any needed assistance in responding to regulatory audits.

10.8 Sponsor Auditing

Sites participating in the TactiFlex PAF IDE clinical investigation will be audited as follows:

1. The Sponsor shall prepare an audit plan as well as the operating procedures for the related duties, and conduct audits in accordance with the audit plan and the operating procedures.
2. Individual engaged in auditing (hereinafter referred to as "auditor") shall be different than those in charge of medical device development or monitoring.
3. The auditor shall prepare an audit report documenting the matters confirmed in the audit to certify and verify that the audit has been conducted and submit them to the Sponsor.

10.9 Committees

10.9.1 Steering Committee

Abbott has established a Steering Committee to advise the Sponsor on key aspects related to the development, execution, analysis, reporting, and overall conduct of the TactiFlex PAF IDE clinical study. The Steering Committee is assigned by the Sponsor, consists of investigators, and serves as an independent advisory board during the planning and execution of the clinical study as well as after its completion. The Sponsor is also represented at committee meetings. Meeting minutes from this committee will be filed with the sponsor.

10.9.2 Publications Committee

A Publication Committee may be established to oversee clinical investigations publications, including publication planning and authorship determinations. Publication Committee membership may include members of the Steering Committee, Principal Investigators, a representative of the Sponsor and a statistician. The Publication Committee will determine policy and strategies regarding individual presentations and/or publications arising from clinical investigation generated data. The committee will also review all external requests for accessing clinical investigation-related data and strategies aligning with the Sponsor's presentation and publication team expectations. The committee will also follow the Sponsor's applicable policies and Standard Operating Procedures.

10.9.3 Data Safety Monitoring Board (DSMB)

The Data Safety Monitoring Board (DSMB) is an independent multidisciplinary group restricted to individuals free of apparent significant conflicts of interest. The source of these conflicts may be financial, scientific, or regulatory in nature. The DSMB is typically composed of at least two physicians with experience relevant to the clinical investigation and a biostatistician.

The DSMB will serve in an advisory role to the Sponsor to ensure safety by reviewing cumulative data from the clinical investigation at prescribed intervals for the purpose of safeguarding the interests of enrolled subjects and those patients yet to be enrolled, as well as the continuing validity and scientific merit of the clinical investigation. The composition, frequency of the meetings and the statistical monitoring guidelines are described in detail in the DSMB charter.

The DSMB may consider a recommendation for modifications or termination of the clinical investigation based on any perceived safety concerns regardless of statistical significance. The recommendations of

the DSMB are not binding, and all final decisions related to clinical investigations modifications rest with the Sponsor

10.9.4 Clinical Events Committee (CEC)

The Clinical Events Committee (CEC) is an independent adjudication body comprised of qualified physicians who are not participants in the clinical investigation. The CEC will review and adjudicate all AEs that are determined by the Sponsor's Safety personnel to potentially meet the criteria of 1) a serious AE and/or 2) an AE related to the investigational devices or ablation procedure. The AE definitions provided in this CIP will be used and the CEC will be governed by a CEC charter. The CEC's adjudication of the reported adverse event data will be used for analysis.

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical investigation.

CRF data collection will be performed through a secure web portal and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

At the conclusion of the clinical investigation, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the investigational sites.

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the IRB/EC and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical investigation.

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to transfer into Sponsor's data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical Investigation, such as the patient's medical condition, treatment, dates of treatment, etc. The Sponsor discloses as part of the clinical investigation informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. Confidentiality of Personal Information will be observed by all parties involved at all times throughout the clinical investigation. The

privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical Investigation data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

11.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data review, data cleaning, and issuing and resolving data discrepancies. If appropriate, the DMP may be updated throughout the duration of the clinical investigation. All revisions will be tracked and document controlled.

11.3 Source Documentation

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. In order to comply with these regulatory requirements/GCP, the following information should be included in the subject record at a minimum and if applicable to the clinical investigation:

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical investigation referencing the Sponsor, CIP number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- CIP-required 12-lead ECGs, reviewed and annotated for clinical significance of out of range results (if applicable).
- Notes regarding CIP-required and prescription medications taken during the clinical investigation (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical investigation
- Any other data required to substantiate data entered into the CRF
- Patient reported outcome measures may be completed using CRF worksheets. These serve as the source documentation.

11.4 Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF completion. The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the

Sponsor on the CRFs and in all required reports. Data on CRFs will be collected for all subjects that are enrolled into the clinical investigation.

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. An electronic audit trail will be used to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical investigation records.

11.6 Investigational Devices Accountability

The Sponsor ships investigational products only to the Principal Investigator (the responsible leader of the investigational site) or his/her legal designee of each site, after sites receive documentation of site activation and shipping authorization is complete.

The Investigator or an authorized designee must maintain adequate records of the receipt and disposition of each investigational device, including part number, batch number, and serial number (if applicable), date used, subject identification, and treating physician. See **Table 1** for a listing of investigational devices by geographic location.

Storage locations for the devices at investigational sites must be locked with access restricted only to investigators and authorized personnel.

Inventory Accountability Log supplied by the Sponsor will be used. The Inventory Accountability Log must document the disposition of all investigational devices including those that have been returned to Sponsor.

All investigational devices that are associated with a device failure or device deficiency must be returned immediately to the Sponsor.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

Institutional Review Board (IRB)/ Ethics Committee (EC) approval for the CIP and ICF/other written information provided to the patient will be obtained by the Principal Investigator at each investigational site prior to consenting and enrolling patients in this clinical investigation. The approval letter must be received prior to the start of this clinical investigation and a copy must be provided to the Sponsor.

Any amendments to the CIP as well as associated ICF changes will be submitted to the IRB/EC and written approval obtained prior to implementation, according to each institution's IRB/EC requirements.

No changes will be made to the CIP or ICF or other written information provided to the patient without appropriate approvals, including IRB/EC, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical investigation is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical investigation, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical investigation, or according to each institution's IRB/EC requirements.

No investigative procedures other than those defined in this CIP will be undertaken on the enrolled subjects without the written agreement of the IRB/EC and the Sponsor.

13.0 CLINICAL INVESTIGATION CONCLUSION

The clinical investigation will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical investigation closure. The final report will be submitted no later than 1-year following the date on which all subjects have either completed the last scheduled follow-up visit or withdrawn from the study.

14.0 PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. Single-center results are not allowed to be published or presented before the multi-center results. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

Upon receiving IDE approval from the FDA, the Sponsor will be responsible for registering this clinical investigation on www.clinicaltrials.gov or any other clinical trials, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical investigation. A full report of the pre-specified outcomes, regardless of the results, will be made public through the ClinicalTrials.gov website no later than 12 months after clinical investigation completion, as required by section 801 of the FDA Amendments Act. If this clinical investigation is terminated early, the Sponsor will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

15.0 RISK ANALYSIS

Risks associated with the TactiFlex SE ablation catheter and EnSite IDE Display Workstation are managed in accordance with ISO 14971. The risk analyses for these devices included objective reviews of published and available unpublished medical and scientific data. The sections below provide an overview of residual risks identified in the risk management reports and anticipated benefits of the medical devices. The additional tests and assessments required by the clinical investigation were analyzed for additional risks and are incorporated in the sections below.

15.1 Anticipated Clinical Benefits

The intended clinical benefit of the TactiFlex™ Ablation Catheter, Sensor-Enabled™ is to provide relief of drug refractory recurrent symptomatic paroxysmal atrial fibrillation.

While there is no guaranteed clinical benefit associated with participation in this study, it is expected that TactiFlex SE will have similar benefits as other commercially available ablation catheters in maintaining sinus rhythm. The clinical benefits of sinus rhythm are well established and include relief of symptoms and improvements in exercise tolerance, hemodynamics, LV function, and quality of life. Restoration of sinus rhythm may confer a mortality benefit.

The EnSite IDE Display Workstation clinical benefits include the diagnosing of complex arrhythmias in cardiac patients as well as mapping prior to the implantation of electrical devices, catheter ablation or surgical ablation, and for the guiding of antiarrhythmic drug-therapy. Compared to the market-released EnSite Velocity v5.2.1 / Ensite Precision v2.2 software, no new labeled or performance claims are being targeted as part of the Precision v2.5 IDE Software release.

The information gathered from this study will also add to the understanding of the treatment options for subjects with paroxysmal AF. This knowledge may advance medical science and have a benefit on other subjects with a similar arrhythmia.

15.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with the TactiFlex SE ablation catheter and the EnSite IDE Display Workstation, and the EP procedure, together with their likely incidence, are described in the Investigator's Brochure. There may be risks related to the device under investigation that are unknown at present. Likewise, the exact frequency of the risk may be unknown.

The following is a list of foreseeable adverse events and anticipated adverse device effects:

- Abnormal vision
- Anesthesia reaction
- Angina/chest pain/discomfort
- Aorto-right atrial fistula
- Arrhythmia, including exacerbation of pre-existing atrial fibrillation
- Arteriovenous fistula
- Bleeding, including major bleeding requiring surgery or transfusion/hematomas/anemia
- Cardiac tamponade
- Cardiovascular injury, including atrial trauma and cardiac perforation
- Coagulation
- Component damage to ICD or implantable pacemaker
- Coronary artery spasm
- Cough
- Cytotoxicity/systemic toxicity/sensitization/endotoxin/pyrogen
- Death
- Dislodgement of implantable cardioverter defibrillator or pacing leads
- Dissection, vessel, coronary artery/pulmonary vein
- Disseminated intravascular coagulation
- Effusion, pericardial
- Effusion, pleural
- Electrical shock/injury
- Elevated cardiac enzymes
- Embolism, air/cardiac/pulmonary/pulmonary vein
- Embolism, material/component
- Endocarditis

- Exacerbation of chronic obstructive pulmonary disease (COPD)
- Fever
- Heart block
- Heart failure
- Hypotension
- Immunological reaction, including anaphylaxis
- Infection
- Laceration
- Left atrial esophageal fistula
- Myocardial infarction
- Organ injury
- Pain, neck/back/groin
- Palpitations
- Pericarditis
- Phrenic nerve injury/diaphragmatic paralysis
- Pneumonia
- Pneumothorax/hemothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary hypertension
- Radiation injury
- Respiratory failure/distress/depression/hypoxia
- Seizure
- Sepsis
- Severe pulmonary vein (PV) stenosis (>70%), or complete occlusion of a PV
- Shock
- Skin burns
- Stiff Left Atrial Syndrome
- Stroke/cerebrovascular accident
- Syncope/vasovagal reaction/dizziness
- Thromboembolism
- Thrombus, including coronary artery/vessel occlusion
- Tissue charring
- Transient ischemic attack (TIA)
- Unintended ablation
- Vagal nerve injury/Gastroparesis
- Valvular damage or insufficiency
- Vessel wall damage
- Volume overload

15.3 Residual Risks Associated with the Device Under Investigation, as Identified in the Risk Analysis Report

Risk analyses for the TactiFlex SE ablation catheter and the EnSite IDE Display Workstation were performed based on risk management plans. The risk analysis process utilizes Failure Mode Effect Analysis (FMEA) tools to systematically identify potential hazards associated with the design and use of the device. Based upon the pre-clinical and bench-testing data for TactiFlex SE and EnSite IDE Display

Workstation, along with clinical data for similar catheter designs (with either contact-force sensing or flexible tips) and market-released EnSite Velocity v5.2.1 / Ensite Precision v2.2 software, all identified residual risks are determined to be within acceptable levels.

The overall residual risk is acceptable given the individual risks are acceptable and the overall benefits outweigh the overall risks.

15.4 Risks Associated with Participation in this Clinical Investigation

Possible risks associated with participating in this clinical study are not anticipated to be any different from risks associated with undergoing procedures with commercially available open-irrigated contact force-sensing RF ablation catheters with electro-anatomical mapping systems. Protocol required assessments are summarized in **Section 6.6.7**. These assessments are standard of care for TactiFlex SE and as such do not pose any additional risks.

15.5 Possible Interactions with Protocol-Required Concomitant Medications

There are no known interactions with concomitant treatments.

15.6 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding patient selection, device handling, and device placement are included in the IFU for TactiFlex SE. It is also stated in the IFU that the devices can only be used by physicians who have received appropriate training on how to use the device. This statement is interpreted to mean that the physician users are expected to be aware of the known and foreseeable safety risks associated with the use of the device including the surgical and/or non-surgical treatment of these conditions.

Risks associated with the use of the devices under investigation are minimized through device design, investigator selection and training, pre-specified patient eligibility requirements, and study monitoring to ensure adherence to the protocol. All adverse events will be reported to the Sponsor as summarized in **Section 7.3** and will be monitored internally for safety surveillance purposes.

Device Design: The TactiFlex SE catheter has a contact force sensor which plays an important factor in achieving transmural lesions that is critical in abolishing the substrate necessary for an arrhythmia and AF in particular. With increasing force, a greater proportion of the electrode surface area is in contact with the tissue, and there is more efficient energy coupling. Gaps in ablation lines are commonly seen when the amount of contact force over the RF delivery time is low and this is associated with higher recurrence rates after ablation for AF. Contact force-sensing ablation catheters such as TactiFlex SE provide a valuable feedback mechanism to help ensure the efficacy of ablation.

TactiFlex SE also utilizes a flexible electrode tip design that has been shown in pre-clinical testing without a contact force sensor [25] to have a lower risk of steam pops during ablation compared to competitive devices. The position of the thermocouple in the flexible tip electrode provides valuable feedback to improve safety.

The catheter also has a magnetic sensor that provides position and orientation information about the catheter to provide information about the direction and magnitude of applied force to the catheter tip electrode and the deflection plane of the catheter. This information is helpful to an operator as they navigate the device in the anatomy. The EnSite IDE Display Workstation has a modified graphical user interface (GUI) that enables the operator to visualize position, orientation, contact force and deflection direction information provided by the catheter's magnetic sensor.

Investigator Selection and Training: Investigators will be selected as outlined in **Section 10.1**. Sites will receive training as stated in **Section 10.4.1**. Additionally, ablating physicians will be qualified and have experience using a contact force sensor as stated in **Section 10.4.2**.

Adherence to the Clinical Investigational Protocol: The clinical study will be monitored by the Sponsor to ensure adherence to the CIP. Subjects will be carefully selected through rigorous screening using pre-specified inclusion and exclusion criteria as stated in **Section 5.2.** Adverse events will be reported to the Sponsor and will be monitored internally for safety surveillance purposes and reported to regulatory authorities as applicable. Adverse events will be adjudicated by qualified physicians who are not participating in the study.

15.7 Risk to Benefit Rationale

Extensive risk analysis and risk mitigation plans (as summarized in **Section 15.3**) has been implemented to minimize any residual risk of the TactiFlex SE catheter and EnSite IDE Display Workstation to subjects. Treatment with TactiFlex SE has all the benefits of a state-of-the-art cardiac ablation therapy with the added benefits of being able to monitor contact force at the catheter tip. The EnSite IDE Workstation has all the benefits of a state-of-the-art electro-anatomical mapping system, while enabling the use of TactiFlex SE for cardiac mapping and ablation procedures. The residual risks are outweighed by the anticipated benefits, as described in the previous sections, and the overall risk has been determined to be acceptable.

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APPENDIX I: ABBREVIATIONS AND ACRONYMS

Acronym/Abbreviation	Description
AAD	Antiarrhythmic drug
ACC	American College of Cardiology
ADE	Adverse device effect
AE	Adverse event
AF	Atrial fibrillation
AFEQT	Atrial Fibrillation Effect on QualiTy of Life
AFL	Atrial flutter
APHRS	Asia Pacific Heart Rhythm Society
AT	Atrial tachycardia
CEC	Clinical Events Committee
CF	Contract force
CFAE	Complex fractionated atrial electrograms
CFR	Code of Federal Regulations (US)
CIP	Clinical investigation plan
CRF	Case report form
CT	Computed tomography
CTI	Cavotricuspid isthmus
CVA	Cerebrovascular accident
DMP	Data Management Plan
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
ECAS	European Cardiac Arrhythmia Society
ECG	Electrocardiogram
EDC	Electronic data capture
EHRA	European Heart Rhythm Association
EMEA	Europe, the Middle East and Africa
EQ	EuroQol Group
ESC	European Society of Cardiology
EU	The European Union
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GUI	Graphical user interface
HIPAA	Health Insurance and Portability and Accountability Act
HRS	Heart Rhythm Society
HSP	High standard power (40-50 Watts)
ICE	Intracardiac echocardiography
ICD	Implantable cardioverter defibrillator
ICF	Informed consent form
ICM	Implantable cardiac monitor
IDE	Investigational device exemption
IFU	Instructions for use
ILR	Implantable loop recorder
INR	International normalized ratio

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Acronym/Abbreviation	Description
IRB	Institutional Review Board
ISO	International Standards Organization
LAA	Left atrial appendage
LAD	Left atrial diameter
LCD	Liquid crystal display
LVEF	Left ventricular ejection fraction
MHRA	Medicines & Healthcare products Regulatory Agency (United Kingdom)
MI	Myocardial infarction
MRI	Magnetic resonance imaging
NIH	National Institutes of Health
NIHSS	National Institutes of Health Stroke Scale
NOAC	Novel oral anticoagulant
NYHA	New York Heart Association
OUS	Outside of the US
PAF	Paroxysmal atrial fibrillation
PCI	Percutaneous coronary intervention
PG	Performance goal
PMA	Pre-market approval
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
PP	Per protocol analysis population
PTE	Per treatment evaluable
PV	Pulmonary vein
RF	Radiofrequency
SADE	Serious adverse device effect
SAE	Serious adverse event
SE	Sensor enabled
SOLAECE	Latin America Society of Electrophysiology and Cardiac Stimulation
SVT	Supraventricular tachycardia
TEE	Transesophageal echocardiogram
TIA	Transient ischemic attack
TTE	Transthoracic echocardiogram
TTM	Transtelephonic monitoring
UADE	Unanticipated adverse device effect
USADE	Unanticipated serious adverse device effect
US	United States of America
WW	Worldwide

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APPENDIX II: DEFINITIONS

The following definitions will be used by the CEC to determine whether the events listed below constitute a device or procedure related serious adverse event included in the primary endpoint. Most of the definitions have been adapted from the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus on AF Ablation [17].

Primary Safety Event	Description
Atrioesophageal fistula	A connection between the atrium and the lumen of the esophagus. Evidence supporting this diagnosis includes documentation of esophageal erosion combined with evidence of a fistulous connection to the atrium, such as air emboli, an embolic event, or direct observation at the time of surgical repair. A CT scan or MRI scan is the most common method of documentation of an atrio-esophageal fistula.
Bleeding	Bleeding is a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in hematocrit.
Cardiac tamponade/perforation	The development of a significant pericardial effusion during or within 30 days of undergoing an AF ablation procedure. A significant pericardial effusion is one that results in hemodynamic compromise, requires elective or urgent pericardiocentesis, or results in a 1-cm or more pericardial effusion as documented by echocardiography. Cardiac tamponade/perforation should also be classified as "early" or "late" depending on whether it is diagnosed during or following initial discharge from the hospital.
Death	Adverse event resulting in the patient's death.
Heart block (AV block)	New, persistent 2nd or 3rd degree AV block not attributable to a vasovagal reaction or medication effect and requiring permanent pacing.
Myocardial infarction	Irreversible necrosis of heart muscle secondary to prolonged ischemia with at least one of the following three criteria: 1. Detection of ECG changes indicative of new ischemia (new ST-T wave changes or new LBBB) that persist for more than 1 hour; 2. Development of new pathological Q waves on an ECG; 3. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
Pericarditis	Pericarditis should be considered a major complication following ablation if it results in an effusion that leads to hemodynamic compromise or requires pericardiocentesis, prolongs hospitalization by more than 48 hours, requires hospitalization, or persists for more than 30 days following the ablation procedure.
Phrenic nerve injury resulting in diaphragmatic paralysis	Phrenic nerve paralysis is defined as absent phrenic nerve function as assessed by a sniff test. A phrenic nerve paralysis is considered to be permanent when it is documented to be present 12 months or longer following ablation.
Pulmonary edema	Excess fluid in the lungs that includes all of the following: • Symptoms (e.g. dyspnea) • Physical findings (e.g. rales, hypoxemia) • Radiologic findings • Response to diuretic therapy • Requires hospitalization
Pulmonary vein stenosis	Reduction of the diameter of a pulmonary vein or a pulmonary vein branch of ≥70% confirmed via imaging (CT or MRI).
Stroke / cerebrovascular accident	Stroke diagnostic criteria: • Rapid onset of a focal or global neurological deficit with at least one of the following: change in level of consciousness, hemiplegia, numbness or sensory loss affecting one side of the body, dysphasia or aphasia, hemianopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke • Duration of a focal or global neurological deficit ≥24 hours; OR <24 hours if therapeutic intervention(s) were performed (e.g. thrombolytic therapy or

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Primary Safety Event	Description
	intracranial angioplasty); OR available neuroimaging documents a new hemorrhage or infarct; OR the neurological deficit results in death. • No other readily identifiable non-stroke cause for the clinical presentation (e.g. brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences). • Confirmation of the diagnosis by at least one of the following: neurology or neurosurgical specialist; neuroimaging procedure (MRI or CT scan or cerebral angiography); lumbar puncture (i.e. spinal fluid analysis diagnostic of intracranial hemorrhage)
Thromboembolism	An arterial or venous thrombus that results in deep vein thrombosis, pulmonary embolism, or peripheral arterial embolism.
Transient ischemic attack	New focal neurological deficit of vascular (occlusive) origin with rapid symptom resolution (usually 1 to 2 hours), always within 24 hours determined by the consulting neurologist; neuroimaging without tissue injury.
Vagal nerve injury/gastroparesis	Vagal nerve injury is defined as injury to the vagal nerve that results in esophageal dysmotility or gastroparesis. Vagal nerve injury is considered to be a major complication if it prolongs hospitalization, requires hospitalization, or results in ongoing symptoms for more than 30 days following an ablation procedure
Vascular access complication	Vascular access complications include development of a hematoma, an AV fistula, or a pseudoaneurysm. A major vascular complication is defined as one that requires intervention, such as surgical repair or transition, prolongs the hospital stay, or requires hospital admission.

APPENDIX III: SITE CONTACT INFORMATION

Contact information for each participating clinical site is available under separate cover by contacting the Sponsor.

APPENDIX IV: LABELS

Copies of all current labeling and Instructions for Use documents for investigational devices listed in **Section 2.2.3** will be provided under separate cover.

APPENDIX V: CASE REPORT FORMS

Final draft case report forms (CRFs) will be provided to FDA under Separate Cover as part of the IDE Submission.

APPENDIX VI: INFORMED CONSENT FORM

A template informed consent form will be provided under separate cover.

APPENDIX VII: MONITORING PLAN

A copy of the Monitoring Plan can be obtained upon request from the Sponsor Clinical Project Manager for the clinical investigation.

APPENDIX VIII: SPONSOR'S CLINICAL SAFETY GROUP CONTACT INFORMATION

APPENDIX IX: REVISION HISTORY

This CIP may be amended as appropriate by the Sponsor. Rationale will be included with each amended version in the revision history table below. The version number and date of amendments will be documented.

IRB/EC and relevant Regulatory Authorities, if applicable, will be notified of amendments to the CIP.

Amendment Number	Version	Date	Details	Rationale
Not Applicable	A	29-May-2020	Initial release of CIP	N/A

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APPENDIX X: CIP SUMMARY

Clinical Investigation Name	TactiFlex PAF IDE [redacted]
Title	Safety and Effectiveness of TactiFlex™ Ablation Catheter, Sensor Enabled™ (TactiFlex SE) for the Treatment of Drug Refractory, Symptomatic, Paroxysmal Atrial Fibrillation (TactiFlex PAF IDE Trial)
Objectives	The primary objective of the TactiFlex PAF IDE clinical trial is to demonstrate that ablation with the TactiFlex Sensor-Enabled™ Ablation Catheter (TactiFlex SE), in conjunction with a compatible RF generator and three-dimensional mapping system, is safe and effective for the treatment of drug refractory, symptomatic paroxysmal atrial fibrillation (PAF) when following standard electrophysiology mapping and radiofrequency (RF) ablation procedures. The TactiFlex PAF IDE clinical trial has two secondary objectives: 1. To provide supporting data for the safety and effectiveness of using TactiFlex SE at 40-50 Watts in the left atrium as part of an AF ablation procedure. 2. To provide supporting data for the safety and effectiveness of using TactiFlex SE to treat cavo-tricuspid isthmus (CTI)-dependent (or "typical") atrial flutter (AFL) through the ablation of the CTI in the right atrium. This data may be used to support an expanded indication for the treatment of CTI-dependent AFL.
Devices Under Investigation	Worldwide: • TactiFlex Ablation Catheter, Sensor Enabled • EnSite IDE Display Workstation (including Investigational Software Precision v2.5) • TactiSys™ Quartz, TactiFlex™ Ablation Catheter SE RF Cable United States Only: • Ampere™ Generator (commercial device that is investigational when used in this study) • TactiSys™ Quartz Equipment (commercial device that is investigational when used in this study)
Number of Subjects Required	Three hundred fifty-five (355) subjects will be enrolled in this clinical investigation. Three hundred five (305) subjects will be enrolled in the main study and 50 subjects will be enrolled in the HSP substudy.
Clinical Investigation Design	Prospective, non-randomized multi-center clinical investigation. Design includes a main study and a separate substudy. Subjects in the main study are to be treated using the full range of ablation power settings in the IFU. Subjects in the substudy are to be treated in the upper end of the recommended ablation power settings (40-50 Watts).
Primary Safety Endpoint	The primary safety endpoint is the rate of device and/or procedure-related serious adverse events with onset within 7-days of any ablation procedure that uses the TactiFlex SE catheter (initial or repeat procedure performed between 31-80 days of initial procedure) that are defined below: • Atrio-esophageal fistula[1]

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	• Cardiac tamponade/perforation[1] • Death • Heart block • Myocardial infarction • Pericarditis • Phrenic nerve injury resulting in diaphragmatic paralysis • Pulmonary edema • Pulmonary vein stenosis[1] • Stroke/cerebrovascular accident • Thromboembolism • Transient ischemic attack • Vagal nerve injury/gastroparesis • Vascular access complications (including major bleeding events[2]) 1. Atrio-esophageal fistula, cardiac tamponade/perforation and pulmonary vein stenosis will be evaluated through 12-months. 2. Bleeding is a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in hematocrit.
Primary Effectiveness Endpoint	The primary effectiveness endpoint for this clinical trial is freedom from documented (symptomatic or asymptomatic) AF/AFL/AT episodes of >30 seconds duration that are documented by 12-lead ECG, transtelephonic monitoring (TTM) or Holter monitor after the initial catheter ablation procedure through 12-months of follow-up (9 months after a 90-day blanking period). AF/AFL/AT recurrence during the 90-day blanking period (≤90 days post-initial procedure) will not be considered a treatment failure. One repeat procedure will be allowed for ablation of AF/AFL/AT recurrence 31-80 days after the initial procedure and will not be considered a treatment failure. Failure to achieve acute procedural success (confirmation of entrance block after a 20-minute minimum waiting period) during the last ablation procedure[1] with the TactiFlex SE catheter will constitute failure to achieve this endpoint. After the 90-day blanking period, use of Class I or III AADs will not count as a therapy failure provided that only previously failed Class I or Class III AADs are taken at doses that do not exceed the previously failed dose. AF/AFL/AT recurrence will only be assessed by 12-lead ECG, TTM, and Holter monitoring devices for assessment of this primary endpoint so that all subjects are monitored equally with devices of the same sensitivity and specificity (recurrence data collected from other devices such as pacemakers, ICDs, or ICMs will not be included in the assessment). ECG, TTM, and Holter data collected from sites will be evaluated by a core laboratory to ensure independent and unbiased assessment of AF/AFL/AT recurrence for endpoint analysis. 1. For subjects that have a repeat ablation procedure ≤80 days after the initial procedure, only failure to achieve acute procedural success during the repeat procedure will contribute to primary effectiveness endpoint.

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Powered Secondary Endpoints	**AAD-Free Secondary Effectiveness Endpoint** The AAD-Free Secondary Effectiveness Endpoint has the same definition as the Primary Effectiveness endpoint, except that any use of Class I or III AADs after the 90-day blanking period will count as a therapy failure in this analysis. **Single-Procedure Secondary Effectiveness Endpoint** The Single-Procedure Secondary Effectiveness Endpoint has the same definition as the Primary Effectiveness endpoint, except that any repeat ablation in the left atrium will count as a failure. **Symptomatic Secondary Effectiveness Endpoint** The Symptomatic Secondary Effectiveness Endpoint has the same definition as the Primary Effectiveness endpoint, except that documented recurrence without documented evidence of symptoms after the 90-day blanking period will not count as a therapy failure in this analysis.
HSP Substudy Endpoints	The endpoints for the HSP substudy will be defined the same as the Primary and Secondary Endpoints for the main study. Results will be reported descriptively using summary statistics. No pre-specified hypothesis testing will be performed. The following as-treated analyses will be performed using the Primary and Secondary Endpoint results from main study and HSP substudy subjects. 1. Results will be summarized separately for subjects that have time-averaged power settings of ≥40 Watts vs. <40 Watts in the left atrium. 2. Results will be summarized separately for subjects that have ≥50% vs. <50% of lesions in the left atrium with power settings ≥40 Watts. 3. Results will be summarized separately for subjects that have ≥25% vs. <25% of lesions in the left atrium with power settings ≥40 Watts.
Subject Follow-up	Baseline, Procedure, Pre-Discharge, 7-day, 5-week, 3-month, 6-month, 12-month • The 7-day, 5-week, and 6-month visits are phone calls to the subject • Baseline, Procedure, Pre-Discharge, 3-month, and 12-month visits are in-person
Inclusion Criteria	1. Plans to undergo a catheter ablation procedure due to symptomatic PAF that is refractory or intolerant to at least one Class I or III antiarrhythmic drug. 2. Physician's note indicating recurrent self-terminating AF 3. One electrocardiographically documented AF episode within 12-months prior to informed consent/enrollment. Documented evidence of the AF episode must either be continuous AF on a 12-lead ECG or include at least 30 seconds of AF from another ECG device. 4. At least 18 years of age 5. Able and willing to comply with all trial requirements 6. Informed of the nature of the trial, agreed to its provisions and has provided written informed consent as approved by the Institutional Review Board/Ethics Committee (IRB/EC) of the respective clinical trial site.
Exclusion Criteria	1. Persistent or long-standing persistent atrial fibrillation 2. Active systemic infection 3. Known presence of cardiac thrombus 4. Hypertrophic cardiomyopathy 5. Arrhythmia due to reversible causes including thyroid disorders, acute alcohol intoxication, and other major surgical procedures in the 90-day period preceding procedure

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	6. Myocardial infarction (MI), acute coronary syndrome, percutaneous coronary intervention (PCI), or valve or coronary bypass grafting surgery within 90 days of procedure 7. Left atrial diameter > 5.0 cm measured within 180 days of procedure (echocardiography or CT) 8. Left ventricular ejection fraction < 35% measured within 180 days of procedure (echocardiography or CT) 9. New York Heart Association (NYHA) class III or IV 10. Previous left atrial surgical or catheter ablation procedure 11. Left atrial surgical procedure or incision with resulting scar (including LAA closure device) 12. Previous tricuspid or mitral valve replacement or repair 13. Heart disease in which corrective surgery is anticipated within 180 days after the procedure 14. Bleeding diathesis or suspected pro-coagulant state 15. Contraindication to long term anti-thromboembolic therapy 16. Presence of any condition that precludes appropriate vascular access 17. Renal failure requiring dialysis 18. Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled with pre-medication 19. Severe pulmonary disease (e.g., restrictive pulmonary disease, constrictive or chronic obstructive pulmonary disease) or any other disease or malfunction of the lungs or respiratory system that produces severe chronic symptoms 20. Women who are pregnant or breastfeeding 21. Presence of other anatomic or comorbid condition that, in the investigator's opinion, could limit the patient's ability to participate in the clinical trial or to comply with follow up requirements, or impact the scientific soundness of the clinical trial results 22. Patient is currently participating in another clinical trial or has participated in a clinical trial within 30 days prior to screening that may interfere with this clinical trial 23. Patient is unlikely to survive the protocol follow up period of 12-months after the procedure 24. Body mass index > 40 kg/m^2 25. Presence of other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results. 26. Individuals without legal authority 27. Individuals unable to read or write 28. Patients who have had a ventriculotomy or atriotomy within the preceding 4 weeks of procedure, 29. Patients with prosthetic valves, 30. Patients with a myxoma, 31. Patients with an interatrial baffle or patch as the transseptal puncture could persist and produce an iatrogenic atrial shunt 32. Patient unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation 33. Stroke or TIA (transient ischemic attack) within the last 90 days 34. Stent, constriction, or stenosis in a pulmonary vein. 35. Rheumatic heart disease 36. Severe mitral regurgitation (regurgitant volume ≥ 60 mL/beat, regurgitant fraction ≥ 50%, and/or effective regurgitant orifice area ≥ 0.40cm^2).

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APPENDIX XI: GERMAN HANDLING OF SERIOUS ADVERSE EVENTS

The scope of this section is to implement the reporting obligation in accordance with §3, section 5 of the German MPSV (Medical Products Safety Ordinance), taking into consideration that notification must be done immediately in accordance § 5, section 2 of the MPSV.

1. Definition of SAE according to §2, Section 5 MPSV:
   Serious Adverse Event: any untoward event occurring within a clinical investigation requiring authorization, which directly or indirectly led to, or which might have led or could lead to death or a serious deterioration in the health of the patient, a user or other person, without taking into account whether the event was caused by the medical device.

2. Notification of SAEs:
   - As soon as the investigator becomes aware of an SAE during the course of a study, the sponsor (Abbott) must be informed immediately, and in no case later than 72 hours after becoming aware.
   - The sponsor (Abbott) also has the obligation to inform the BfArM of all SAEs according to following table.

<table>
<tr><th>Condition for reporting to BfArM</th><th>Country of occurrence</th><th>Timeline for reporting to BfArM</th><th>Form</th></tr>
<tr><td rowspan="2">a causal relationship between the SAE and the investigational medical device, a comparator device, diagnostic or therapeutic procedures performed as part of the clinical trial or other conditions of the trial conduct cannot be excluded</td><td>Germany</td><td>immediately</td><td>German SAE Report Form (latest version) for single reports</td></tr>
<tr><td>all other countries where the clinical trial is performed</td><td>immediately</td><td>MEDDEV 2.7/3 Report Table

Please document all SAEs cumulatively on the same spreadsheet

Report to be sent to mpsae@bfarm.de</td></tr>
<tr><td rowspan="2">a causal relationship between the SAE and the investigational medical device, a comparator device, diagnostic or therapeutic procedures performed as part of the clinical trial or other conditions of the trial conduct can be excluded</td><td>Germany</td><td>quarterly</td><td rowspan="2">• Quarterly Report Template V1.0
• Table Complication Rates
• MEDDEV 2.7/3 Report Table

Please document all SAEs cumulatively on the same spreadsheet

Report to be sent to mpsae@bfarm.de</td></tr>
<tr><td>all other countries where the clinical trial is performed</td><td>quarterly</td></tr>
</table>

- The German SAE Report Form is available on the BfArM homepage: http://www.bfarm.de/DE/Medizinprodukte/form/functions/formmp-node.html

- Please note that the SAE gets a unique ID which consists of 4 Parts:
  - The Study Code [redacted]
  - The Center ID (ORACLEID = Center Name)
  - The Patient No
  - The Date of SAE in the format (Year (2-digits) Month Day) (Example: CRD_858_EU0284_01_160203 for an event which occurred on 3 February for Patient 1 in center EU0284 within the Study CRD_858).
- The German Quarterly Report Template is available on the BfArM Homepage: http://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/SAE_Berichtsvorlage.docx
  Table Complication Rates http://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/SAE_Komplikationsrate.xlsx
  Instructions for completing the quarterly assessment form for serious adverse events http://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/SAE_Berichtsvorlage_Hinweisblatt.pdf

- The investigator will be instructed on this obligation during the initiation visit.
- Information about the obligation must be documented in the "training log".
- Written confirmation that this working procedure has been passed on to the trial center is sent to the investigator and then attached to the study file.

3. Responsibility of the investigators:
   - The investigator has to notify the SAE to the sponsor without undue delay.
   - SAEs should be reported either by
     i. EDC (primary reporting tool)
     ii. E-Mail: [redacted]
   - The investigator or main investigator is obliged to respect the deadline for notification of SAEs.
   - A person within the study center will be designated to collect the necessary information.
   - A person within the study center will be designated to pass on this information to the sponsor. A list of people (including a representative) will be prepared for this purpose.

4. Responsibilities of the monitor (Abbott):
   - The monitor will be instructed of his/her responsibilities with regard to SAEs.
   - If the monitor discovers an SAE during the course of the study that was not notified or not notified within the notification deadline, the sponsor's action plan will take effect. The BfArM is then notified of the SAE without undue delay and the investigator is informed of it straight away.

5. Responsibilities of the Sponsor
   - The Sponsor (Abbott) shall notify any SAEs without undue delay (at the latest however within 3 calendar days) after awareness.
   - A person will be designated to verify SAEs that occur during the clinical study.
   - A list of Abbott people who shall be informed about SAEs is to be drawn up.
   - A person will be designated who is responsible for the assessment of any SAEs.

- A person or team will be designated who is responsible for initiating corrective actions if necessary.

6. Responsibilities of the sponsor in Germany
   - All people within Abbott Medical GmbH who are involved in this clinical study be will instructed of the notification deadlines and are obliged to respect them.
   - SAEs/PERs (Product Event Reports) are coordinated by Clinical Safety or by [redacted] (Manager Field Clinical Submission Specialists, Germany).
   - SAE notifications to the BfArM are to be made by Clinical Safety.
   - Vigilanz-Responsible for this study: [redacted] (Manager Field Clinical Submission Specialists, Abbott Medical GmbH, Germany)
     Phone: [redacted]

7. Notification of SAEs in other countries
   - A list of the EU countries or other geographies with potential study sites outside of Germany are listed below. SAEs will also be reported in the EU countries or other geographies that have sites participating in this clinical investigation.
     - Australia
     - Austria
     - Canada
     - Czech Republic
     - Denmark
     - France
     - Holland
     - Hong Kong
     - Italy
     - Poland
     - Serbia
     - Spain
     - Taipei
     - United Kingdom
     - United States