FARAPULSE

FARA-Free:
A Single Arm Pilot Study of
Pulsed Field Ablation in the Treatment of
Paroxysmal Atrial Fibrillation

CLINICAL INVESTIGATION PLAN (CIP) NUMBER: CS0766 REVISION C

SPONSOR:
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ISSUE DATE: 13 FEBRUARY 2020

This study is to be performed in accordance with Good Clinical Practice (GCP), the ethical principles that have their origin in the Declaration of Helsinki, International Conference on Harmonisation E6 and ANSI / AAMI / ISO Standards 14155:2011.

Revision Letter	Change Description
A	Initial Release
B	• Updated to add First-in-Human FARADRIVE Sheath and revised system name • Added additional study investigator information • Added roll in subjects to Section 5.6 Populations for Analysis • Added Section 9.2.5 Sharing New Information
C	• Addition of Recording Switch Box as accessory to the FARASTAR Generator • Updated system components figure (Figure 1) • Addition of Section 3.10.6 – Treatment of Pregnancies Identified During Subject Participation • Added Document Revision History Table • Update Figure 5 – new figure of the FARADRIVE sheath and dilator

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Executive Summary

SPONSOR NAME:	FARAPULSE, Inc.
TITLE OF STUDY:	FARA-Free: A Single Arm Pilot Study of Pulsed Field Ablation in the Treatment of Paroxysmal Atrial Fibrillation
CIP NUMBER / REVISION:	CS0766 Revision C
OBJECTIVE:	The objective of this pilot study is to confirm that endocardial ablation using the FARAPULSE Ablation System Plus with commercial design devices is both safe and effective for treating drug-resistant paroxysmal atrial fibrillation (PAF).
CLINICAL HYPOTHESIS:	Pulmonary vein isolation (PVI) and related ablations created by the FARAPULSE Ablation System Plus are a safe and effective treatment for drug resistant paroxysmal atrial fibrillation (AF).
NAME OF INVESTIGATIONAL DEVICE:	FARAPULSE Ablation System Plus (commercial design) • FARAWAVE™ Endocardial Ablation Catheters • FARAFLEX™ Endocardial Ablation Catheter • FARASTAR™ Endocardial Generator • FARADRIVE™ Steerable Sheath • FARADRIVE™ Deflectable Sheath
STUDY OVERVIEW:	This is a prospective, multi-center, single arm safety and effectiveness pilot study. Subjects will undergo percutaneous PFA ablation for pulmonary vein isolation and at the clinical discretion of the investigator receive PFA ablation of additional arrhythmogenic locations. Subjects will be followed at 7 days (telephonic), 30 days, 90 days, 6 months and 12 months for adverse events, recurrence of arrhythmia after a 90-day Blanking Period and other relevant outcome measures.
STUDY POPULATION:	Subjects with documented drug-resistant (Class I-IV) symptomatic PAF who have had ≥ 2 episodes within 6 months of enrollment.

PLANNED ENROLLMENT:	Up to 50 subjects at up to 6 European centers with no more than 15 subjects being enrolled at any one site. Two (2) subjects at each new site may be roll in subjects, reported but not included in pilot analysis. All safety and effectiveness results from roll in patients will be fully reported in clinical study reports, but effectiveness results from these patients will not be included in statistical calculation of per protocol endpoints. 50 subjects with a targeted enrollment of at least 30 at new sites which have not used a PFA system before, utilizing the updated commercial design investigative devices allows assessment of the revised devices, confirms trial parameters and provides feedback on the training and oversight of new investigators. The following sites will not have performed PFA ablation using a FARAPULSE system at the time of enrollment in this trial: Dr. Mattias Duytschaever AZ Sint-Jan Ruddershove 10 8000 Bruges, Belgium +32 50 45 21 11 Pr. Josef Kautzner IKEM Videnska 1958/9 140 21 Prague 4 Czech Republic Tel: +420 236 051 111

DESIGN:	Prospective, single arm, open label, multi-center pilot study utilizing the FARAPULSE Ablation System Plus to treat subjects with PAF. Subjects will undergo percutaneous ablation for pulmonary vein isolation and potential CTI and additional lesions. A single re-ablation with the experimental devices during the blanking period (through Day 90) is permitted but does not extend either the blanking period or the total follow-up interval. **Safety:** Subjects will then be followed at 7 days (telephonic), 30 days, 90 days, 6 months and 12 months for adverse events. A composite device and procedure related SAE rate will be reported and compared to a performance goal. **Effectiveness:** Subjects will be monitored with weekly scheduled and symptom-driven unscheduled event monitoring, as well as 6 and 12-month 24 hour Holter monitoring, for recurrence of arrhythmia after a 90 day blanking period. The freedom from recurrent atrial tachyarrhythmias (ATA) through 12 months will be reported and compared to a performance goal.
DURATION OF SUBJECT PARTICIPATION:	Site initiation and investigator training is estimated to take 3 months. The enrollment period is estimated to take 4 months and subjects will be followed for up to 13 months. Procedural and 7-day data for regulatory submission should be available approximately 5 months after first enrollment. The total study duration will be approximately 20 months from the beginning of site training to final study follow-up.
PLANNED PROCEDURES:	**PVI:** Subjects will undergo an attempt to isolate all pulmonary veins or their anatomic equivalent. **CTI:** Subjects with a past history of atrial flutter, who are at risk of atrial flutter, who present with atrial flutter during the Index Procedure or who have inducible cavo-tricuspid isthmus-mediated (typical) flutter may undergo ablation of the cavo-tricuspid isthmus at the discretion of the investigator. **Other:** Additional lesions may be made at the discretion of the investigator to target focal sites and/or electrical gaps following attempted pulmonary vein isolation.

PRIMARY SAFETY ENDPOINT:	The primary safety endpoint for this study is the Composite Safety Endpoint (CSE) defined as the incidence of the following serious adverse events (SAEs) which are device- or procedure-related, as adjudicated by the CEDMC based on the definitions contained in the Composite Safety Endpoint Definitions Table 4. <u>Early onset (within 7 days of an index or protocol-specified reablation procedure)</u> • Death • Myocardial infarction • Persistent diaphragmatic paralysis • Stroke • Transient ischemic attack • Peripheral or organ thromboembolism • Pericardial effusion, hemorrhage or tamponade • Vascular access complications • Hospitalization • Heart block <u>Late onset (any time during follow-up)</u> • Pulmonary vein stenosis • Atrio-esophageal fistula
PSE STATISTICS	The proportion of study subjects with one or more PSEs will be reported and compared descriptively to historical data.
ADDITIONAL SAFETY ANALYSES:	The proportion of subjects: 1. With any adverse event in the Composite Safety Endpoint definitions table, whether or not adjudicated as an SAE 2. With a device- or procedure-related SAE 3. With a device- or procedure-related stroke or TIA 4. With a pre-post cranial MRI change (brain imaging subpopulation) 5. Requiring cardioversion 6. Requiring an arrhythmia-related hospitalization Learning curve analysis.

PRIMARY EFFECTIVENESS ENDPOINT:	The proportion of subjects with:
	• Acute Procedural Success, AND
	• Therapeutic Success, defined as freedom from:
	  ○ Post blanking period through assessment: occurrence of AF, AFL or AT, or ablation for AF/AFL/AT using the study device
	  ○ At any time: ablation for AF/AFL/AT with a nonstudy device
	Therapeutic success will be assessed between Day 91 and the 12 month ± 4 week follow-up visit.

ADDITIONAL EFFECTIVENESS ANALYSES:	1. Acute Procedural Success, defined as the percutaneous endocardial creation of an electrically isolating set of lesions around the ostia of pulmonary veins (PV) during the index procedure, as clinically assessed by entrance and/or exit block performed ≥ 20 minutes after the last PVI lesion is made on a per patient basis. 2. The primary effectiveness endpoint for subjects not on AFDs between Day 105 and the 12 month follow-up visit. 3. First pass isolation (index procedure) consisting of Acute Procedural Success after a single planned set of lesions in each attempted PV 4. The proportion of subjects with early recurrence of atrial fibrillation (ERAF) by 90 days after the initial study ablation 5. The proportion of attempted subjects that achieve Acute CTI Success, defined as the creation of bi-directional electrical block across the cavo-tricuspid isthmus using the investigational devices. 6. Learning curve analysis 7. Rate of any reablation through 12 months of follow-up

PROCEDURAL ASSESSMENTS:	1. Assessments of duration for procedure components
	  a. Procedure time (initiation of venous access to venous access closure).
	  b. Dwell time (sum of catheter entry-to-exit durations).
	  c. Total ablation time (first ablation to last ablation)
	  d. Fluoroscopy time (total duration of exposure).
	2. Characterization of lesion sets:
	  a. PVI ablations
	  b. Extra-PV ablations, excluding CTI ablations
	  c. CTI ablations
	  d. Anomalous PV ablations

QUALITY OF LIFE MEASURES	Subjects will undergo assessment with the EQ-5D-3 L instrument at baseline and 12 months.

INCLUSION CRITERIA:	Study subjects are required to meet all the following inclusion criteria to participate in this study: 1. Patients with documented drug resistant symptomatic PAF meeting all three of the following criteria: a. Confirmed AF: Documentation may include a recording such as ECG, transtelephonic monitor (TTM), Holter monitor, implanted devices, or telemetry strip, recorded within one year prior to enrollment and showing at least 30 seconds of AF. b. Frequent AF, defined as ≥ 2 episodes within 6 months of enrollment. c. Failed atrial fibrillation drug (AAD) treatment, meaning therapeutic failure of at least one AAD (class I – IV) for efficacy and / or intolerance. 2. Patients who are ≥ 18 and ≤ 75 years of age on the day of enrollment. 3. Patient participation requirements: a. Lives locally. b. Is willing and capable of providing Informed Consent to undergo study procedures. c. Is willing to participate in all examinations and follow-up visits and tests associated with this clinical study.

EXCLUSION CRITERIA:	Subjects will be excluded from participating in this study if they meet any one of the following exclusion criteria: 1. Atrial fibrillation that is any of the following: a. Persistent (by diagnosis or continuous duration > 7 days) b. Secondary to electrolyte imbalance, thyroid disease, alcohol or other reversible / non-cardiac causes c. Requires ≥ 4 cardioversions in the preceding 12 months 2. Left atrial anteroposterior diameter ≥ 5.0 cm as documented by transthoracic echocardiography (TTE) or computed tomography (CT) 3. At any time, one or more of the following cardiac procedures, implants or conditions: a. Clinically significant arrhythmias other than AF, AFL or AT b. Any previous endocardial or epicardial ablation or surgery for AF c. Hemodynamically significant valvular disease d. Any prosthetic heart valve e. Heart failure – any of the following: i. NYHA Class III or IV CHF ii. LVEF <40% iii. Heart failure hospitalization f. Atrial or ventricular septal defect closure g. Atrial myxoma h. Left atrial thrombus i. Left atrial appendage device or occlusion j. Pacemaker, implantable cardioverter defibrillator or cardiac resynchronization therapy devices k. Significant or symptomatic hypotension l. Bradycardia or chronotropic incompetence m. History of pericarditis n. History of rheumatic fever o. History of congenital heart disease with any residual anatomic or conduction abnormality p. Any pulmonary vein abnormality, stenosis or stenting 4. Any of the following cardiovascular procedures, implants or conditions within the specified interval related to the date of enrollment: a. Within the 3 months preceding enrollment: i. Myocardial infarction ii. Unstable angina iii. Percutaneous coronary intervention iv. Treatment with amiodarone

EXCLUSION CRITERIA (CONTINUED):	b. Within the 6 months preceding enrollment: i. Heart surgery ii. Stroke or TIA iii. Any thromboembolic event iv. Carotid stenting or endarterectomy v. Pericarditis or pericardial effusion c. Within the 12 months following enrollment: i. Any likelihood of cardiac surgery or transplant 5. History of blood clotting or bleeding abnormalities 6. Contraindication to, or unwillingness to use, systemic anticoagulation 7. Contraindications to both CT and MRI 8. Sensitivity to contrast media not controlled by premedication 9. Women of childbearing potential who are pregnant, lactating, not using birth control or planning to become pregnant during the anticipated study period 10. Medical conditions that would prevent participation in the study, interfere with assessment or therapy, significantly raise the risk of study participation, or confound data or its interpretation, including but not limited to: a. Body mass index (BMI) > 40 b. Solid organ or hematologic transplant, or currently being evaluated for an organ transplant c. Severe lung disease, pulmonary hypertension, or any lung disease involving abnormal blood gases or significant dyspnea d. Renal insufficiency with an estimated creatinine clearance < 30 mL/min/1.73 m2, or any history of renal dialysis or renal transplant e. Active malignancy or history of treated cancer within 24 months of enrollment f. Clinically significant gastrointestinal problems involving the esophagus, stomach and/or untreated acid reflux g. Clinically significant infection h. Predicted life expectancy less than one year 11. Clinically significant psychological condition that in the investigator's opinion would prohibit the subject's ability to meet the protocol requirements. 12. Current or anticipated enrollment in any other clinical study.

Abbreviations and Acronyms

ACL	Arrhythmia Core Lab
ACT	Activated clotting time
ADE	Adverse device effect
AE	Adverse Event
AF	Atrial fibrillation
AFD	Atrial Fibrillation Drug
AFL	Atrial flutter
APS	Acute Procedural Success
AT	Atrial tachycardia
BMI	Body Mass Index
CA	Competent Authority
CBC	Complete blood count
CEDMC	Clinical Events and Data Monitoring Committee
CHA_2DS_2-VASc	Termed "CHADS-VASC" a clinical prediction rule for stroke
CHF	Congestive heart failure
CIP	Clinical Investigation Plan
CPS	Chronic Procedural Success
CRF	Includes CRF (case report form) and eCRF (electronic case report form)
CRO	Clinical research organization
CSE	Composite Safety Endpoint
CT	Computed tomography
CTI	Cavo-tricuspid isthmus
DCCV	Direct current cardioversion
EC	Ethics Committee
ECG	Electrocardiogram
ERAF	Early recurrence of atrial fibrillation
ICF	Informed Consent Form
INR	International normalized ratio
IVC	Inferior vena cava
LA	Left atrium or left atrial
MI	Myocardial infarction
MRI	Magnetic resonance imaging
NOAC	Novel oral anticoagulant
NIHSS	National Institutes of Health Stroke Scale
NYHA	New York Heart Association
PAF	Paroxysmal atrial fibrillation
PFA	Pulsed Field Ablation
PT	Prothrombin time
PTT	Partial thromboplastin time
PV	Pulmonary vein
PVI	Pulmonary vein isolation
PVS	Pulmonary vein stenosis
SADE	Serious adverse device effect
SAE	Serious adverse event
TEE	Transesophageal echocardiography

TIA	Transient ischemic attack
TTE	Transthoracic echocardiography
TTM	Transtelephonic monitor
UADE	Unanticipated adverse device effect
USADE	Unanticipated serious adverse device effect

1. Introduction

1.1 Background and Rationale

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting approximately 2.2 million people in the United States and 4.5 million in the European Union.[1, 2]. The incidence increases with advancing age, affecting 6% of the population over age 60 and 10% of the population over age 80[3, 4]. Age-adjusted population trending projects 16 million people in the United States will have AF by 2050[5]. Atrial fibrillation remains a significant cause of morbidity and mortality in industrialized societies. The annual risk of AF related stroke is 5% per year and one of every six strokes diagnosed occurs in the presence of AF.[6] Therefore, patients with AF require long-term anticoagulation to prevent embolic events. Failure to manage AF may also lead to anatomic and electrical remodeling of the left atrium, tachycardia-induced cardiomyopathy, and reduced left ventricular function (heart failure). AF remains an extremely costly public health burden, with annual per patient cost of care approaching €3000 (approximately U.S. $3200).[7]

The Heart Rhythm Society (HRS) 2017 Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation[8] defines several different stages of atrial fibrillation. Paroxysmal AF (PAF) is defined as AF that terminates spontaneously or with intervention within 7 days of onset.

This trial extends the investigation of PAF treatment by FARAPULSE pulsed field ablation in two important ways. Firstly, the devices utilized have been redesigned to be more acceptable in anticipated commercial use. Secondly the protocol has been refined to more closely approximate the data gathering and study procedures that will be necessary for the upcoming randomized pivotal trial.

1.2 Irreversible Electroporation (IRE)

Al-Sakere 2007[9] described irreversible electroporation as a non-thermal tissue ablation technique in which intense short duration electrical fields are used to permanently open pores in cell membranes, thus producing non-thermal tissue ablation. Their study, using a mouse model, showed complete regression in 92% of treated tumors. IRE ablation has a tissue specific mechanism of ablation. The tissue injury from IRE ablation occurs at the cellular level with loss of homeostasis leading to necrosis or apoptosis[10 11 12 13] IRE ablation typically spares the extracellular matrix, which facilitates rapid wound healing.[14, 15, 16, 17, 18]

Thomson 2011[19] reported a case-series study (N=38) assessing the safety of IRE for treating liver, kidney or lung cancers in humans. The first four patients showed signs of transient ventricular arrhythmia, so subsequent patients were all treated using electrocardiogram (ECG)-synchronized deliver of electroporation pulses. There were two further arrhythmias, and two cases of inadvertent damage to neighboring organs. 68% of tumors were completely ablated. The authors concluded that IRE is safe for clinical use, provided ECG-synchronized delivery is used.

A research group led by FHM Wittkampf in Utrecht has been investigating the potential effectiveness and safety of epicardial electroporation in AF ablation procedures using porcine models. Wittkampf 2011[20] (N=10) used a circular ablation

catheter and showed that PVI was achieved in all animals, with no sign of stenosis at 3-week follow up. Van Driel 2014[21] (N=6) confirmed this result out to 3-month follow up. Neven 2014[22] (N=5) showed that electroporation lesion depth depended on the level of electrical energy applied, reaching 8 mm at 300 joules.

Van Driel 2015 (N=20) showed that electroporation could create deep lesions close to the phrenic nerve without damage to the nerve. Neven 2014 similarly showed that neighboring coronary arteries were undamaged by electroporation (N= 5). These animal studies suggest that irreversible electroporation can safely create deep lesions in heart tissue when applied epicardially without harming adjacent tissues.

1.3 Summary of FARAPULSE Clinical Studies

1.3.1 Endocardial Ablation Studies – The IMPULSE Study

FARAPULSE, Inc. initiated a safety and feasibility study at Na Homolce Hospital in Prague, Czech Republic and Hopital Cardiologique du Haut-Leveque in Pessac, France under the "IMPULSE" Protocol, CS0188. This study is being conducted using the FARAPULSE Endocardial Ablation System, functionally the same system which will be used in the subject investigation with the addition of the FARAFLEX catheter (please refer to section 1.5 for more information). Forty (40) patients were enrolled between January and December of 2018. Thirty (30) patients were enrolled in Prague and ten (10) were enrolled in Bordeaux. All patients were discharged in good condition. One patient was treated for tamponade at the conclusion of the Index Procedure and the event was resolved. Three patients were re-hospitalized for atrial arrhythmia and all of these events were resolved. One patient experienced a prolonged Index hospitalization due to an arteriovenous groin fistula which was resolved. At the conclusion of the Index Procedure, all (100%) pulmonary veins (PVs) were isolated using the FARAPULSE Endocardial Ablation System. Thirty-five (35) patients have returned for the protocol-defined 3-month remapping procedure to assess durable PV isolation. Among these patients, 70% of PVs remained isolated at the 3-month remapping procedure. All PVs in fourteen (14) patients remained isolated. These results support the safety and performance of the system.

1.3.2 Endocardial Ablation Studies – The PEFCAT Study

FARAPULSE, Inc. has also initiated a safety and feasibility study at Na Homolce Hospital in Prague, Czech Republic and Hopital Cardiologique du Haut-Leveque in Pessac, France under the "PEFCAT" Protocol, CS0267. This study is being conducted using the FARAPULSE Endocardial Ablation System, functionally the same system which will be used in the subject investigation with the addition of the FARAFLEX catheter (please refer to section 1.5 for more information). Sixty (60) patients have been enrolled between October 2018 and June 2019. Fifty (50) patients were enrolled in Prague and ten (10) were enrolled in Bordeaux. All patients were discharged in good condition. One patient was treated for an air embolism during the Index Procedure and the event was resolved. Three patients were re-hospitalized for atrial arrhythmia and all of these events were resolved. One patient was hospitalized for back pain and the event was resolved. One patient experienced a prolonged Index

hospitalization due to an arteriovenous groin fistula which was resolved. At the conclusion of the Index Procedure, all pulmonary veins (PVs) in all patients were isolated using the FARAPULSE Endocardial Ablation System. Forty-nine (49) patients have returned for the protocol-defined 75-day remapping procedure to assess durable PV isolation. Among these patients, 96% of PVs remained isolated at the 3-month remapping procedure All PVs in thirty-nine (39) patients undergoing reassessment remained isolated. These results support the safety and performance of the system.

1.3.3 Endocardial Ablation Studies – The PEFCAT II Study

FARAPULSE, Inc. has initiated regulatory submissions for the PEFCAT II expanded safety and feasibility study of the FARAPULSE Endocardial Multi Ablation System. This study will investigate PVI and CTI ablation using the FARAWAVE and FARAFLEX catheters. It is expected to commence in October 2019.

1.4 Rationale for Conducting This Feasibility Study

Catheter ablation for PAF with a variety of energy sources and catheter configurations has been demonstrated to be a safe and effective procedure. Prior iterations of the FARAPULSE Ablation System Plus have undergone preclinical and clinical testing to demonstrate that they can isolate pulmonary veins quickly and with minimal complications, using a standard catheter-based endocardial procedure. Ongoing clinical follow-up demonstrates durable lesions at 75-day remapping procedures and freedom from recurrent PAF greater than 85%. Further, the FARAPULSE Ablation System Plus has undergone preclinical testing in representative models to demonstrate that it can isolate pulmonary veins and create other cardiac lesions quickly, durably, and with minimal complications, using a standard catheter-based endocardial procedure.

This study constitutes the final pilot study utilizing both commercially designed devices as well as a trial design that resembles the intended pivotal studies for market approval. Confirmation of the final design and the clinical trial structure is the appropriate next step before starting a large, global, multicenter randomized pivotal study of FARAPULSE PFA technology compared with existing radiofrequency and cryoablation technologies.

2. Investigational Devices

2.1 Names of Investigational Devices

The FARAPULSE Ablation System Plus is comprised of the following devices:

- FARAWAVE Endocardial Ablation Catheter
- FARAFLEX Endocardial Ablation Catheter
- FARASTAR Generator
- FARADRIVE Steerable Sheath
- FARADRIVE Deflectable Sheath

2.2 Intended Use

The FARAPULSE Ablation System Plus is indicated for the treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation.

The FARAFLEX Endocardial Ablation Catheter is used as an adjunctive device in the endocardial treatment of atrial fibrillation with the following intended uses:

- Gap ablation to complete electrical isolation of the pulmonary veins,
- Focal ablation of cardiac arrhythmias, and
- Creation of ablation line between the inferior vena cava and the tricuspid valve.

2.3 Classification

The FARAWAVE Endocardial Ablation Catheter and FARAFLEX Endocardial Ablation Catheter are classified as Class III medical devices. Per MDD 93/42/EEC Annex IX Rule 6 applies to the ablation catheters, which defines the catheters as surgically invasive devices intended for transient use (<60 min) that specifically controls, diagnoses, monitors or corrects a defect of the heart or of the central circulatory system through direct contact with these parts of the body.

The FARASTAR Generator is classified as a Class IIb medical device. Per MDD 93/42/EEC Annex IX Rule 9 applies to the Generator, which defines it as an active therapeutic device that is intended to administer or exchange energy to and from the human body in a potentially hazardous way, taking account of the nature, the density and the site of application of the energy.

The FARADRIVE Steerable Sheath and FARADRIVE Deflectable Sheath are classified as Class III medical devices. Per MDD 93/42/EEC Annex IX Rule 6 applies to the Steerable and Deflectable Sheath Systems, which define them as surgically invasive devices intended for transient use (<60 min) that specifically control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with these parts of the body.

2.4 FARAPULSE Ablation System Plus

The FARAPULSE Ablation System Plus used in the proposed clinical investigation consists of the FARAWAVE Endocardial Ablation Catheter, the FARAFLEX Endocardial Ablation Catheter, the FARASTAR Generator, FARADRIVE Deflectable Sheath, and the FARADRIVE Steerable Sheath. These components, sub-components and model numbers are listed in **Table 1**.

Table 1. FARAPULSE Endocardial Ablation System – Components

Component	Subcomponents	Model Numbers
FARAWAVE Endocardial Ablation Catheter	1. Ablation Catheter (31 mm or 35 mm fully deployed diameter) 2. Extension Cable	41C601 (31 mm) and 41C602 (35 mm) 41C604
FARAFLEX Endocardial Ablation Catheter (adjunctive device)	1. Ablation Catheter (17 mm fully deployed diameter) 2. Extension Cable	41C603 41C604
FARASTAR Generator	1. Pulsed Field Ablation Generator 2. FARASTAR Remote Touch Screen 3. FARASTAR FARASTIM Box 4. FARASTAR FARASTIM Cable 5. FARASTAR EGM Cable 6. FARASTAR Accessories Cable Set 7. Recording Switch Box	61C601 61C602 61C603 61C604 61C605 61C606 61C607
FARADRIVE Steerable Sheath FARADRIVE Deflectable Sheath	1. Sheath and Dilator 1. Sheath and Dilator	21C601 20T401

During the investigation certain CE Marked medical devices may be used in conjunction with the FARAPULSE Ablation System Plus. These are listed in **Table 2**.

Table 2. CE Marked Devices Utilized in Conjunction with FARAPULSE System

CE Marked Devices That May be Used in Conjunction with FARAPULSE Ablation System Plus
St. Jude BRK 98cm Transseptal Needle

A schematic of the FARAPULSE Ablation System Plus is depicted in **Figure 1.**

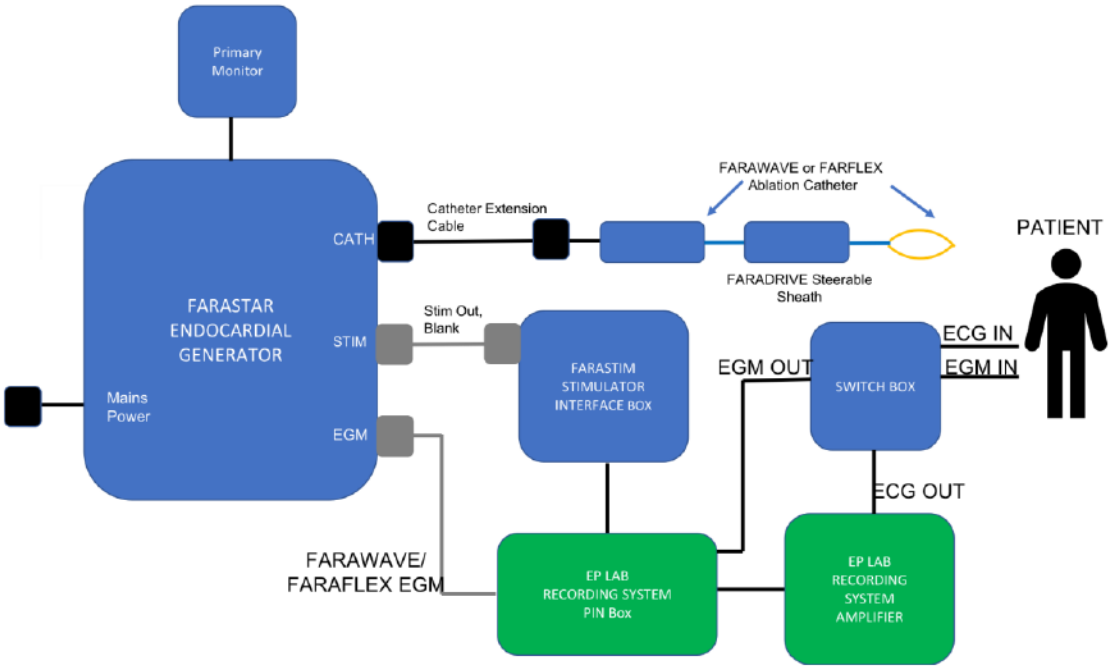

Figure 1. FARAPULSE Ablation System Plus Components

2.4.1 FARAWAVE Endocardial Ablation Catheter

The FARAWAVE Endocardial Ablation Catheter consists of two (2) components: Ablation Catheter and Extension Cable, which are used together. Both components are sterile and single use only.

The ablation catheter is offered in two different sizes: 31 mm (REF 41C601) and 35mm (REF 41C602) deployed diameters, to accommodate varying pulmonary vein anatomy. Selection of either catheter will be at the investigator's discretion.

The Ablation Catheter is a multi-electrode catheter that connects electrically to the Endocardial Generator (**Figure 2**). It consists of a distal section with electrodes arranged on splines, a shaft section, and a proximal handle with a manually operated deployment control. The five splines deploy into a basket-shaped configuration or flower-shaped configuration with five petals (**Figure 3**).

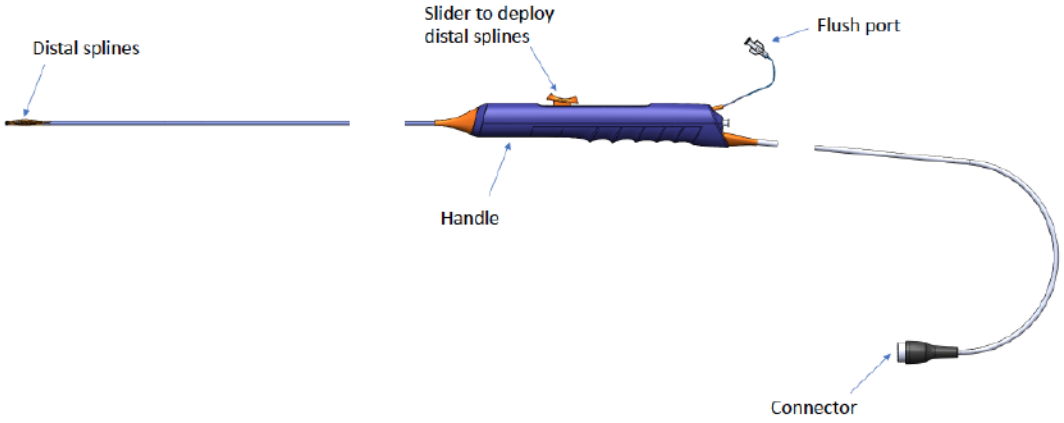

Figure 2. FARAWAVE Endocardial Ablation Catheter

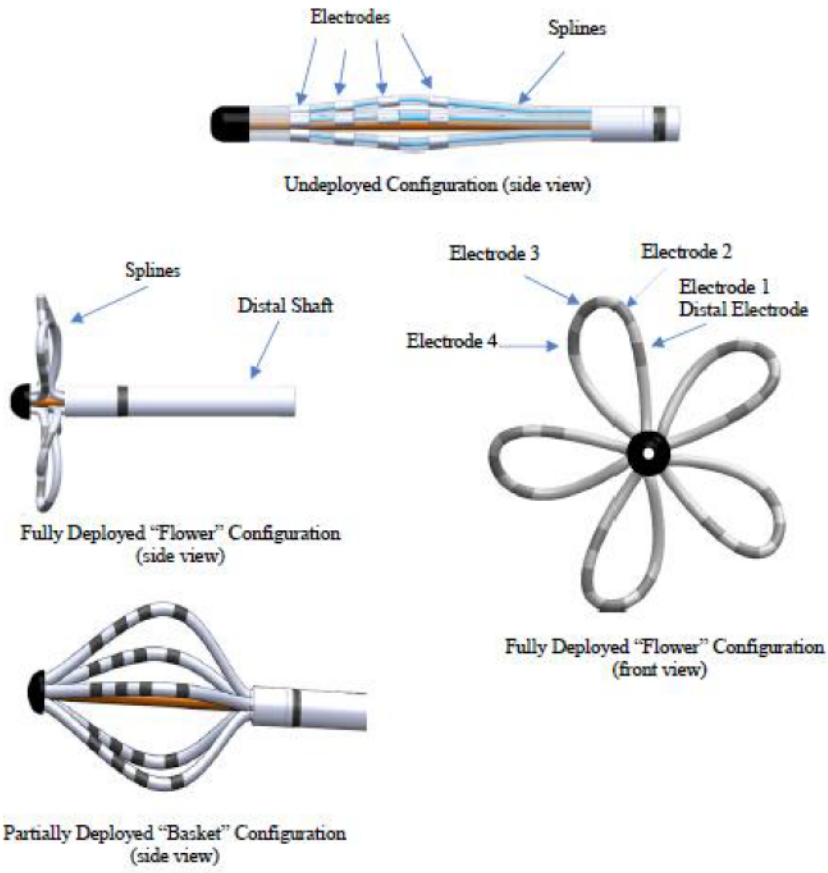

Figure 3. Undeployed (top) and Fully Deployed "Flower" (middle left and right) vs. Partially Deployed "Basket" (bottom left) Configurations of the FARAWAVE Endocardial Ablation Catheter Distal End

Each spline has a single electrode that is separately wired to facilitate connection to a mapping or recording system via a cable supplied with the system. The handle includes a flush port for saline infusion, a deployment control knob with a guidewire lumen hub that can be connected to a hemostasis valve, and a short cable that terminates in a single connector for attachment to the extension cable. The other end of the extension cable attaches to the front panel of the FARASTAR Endocardial Generator. The extension cable is packaged sterile and is single-use only. The Pulsed Field Ablation energy is delivered via the FARASTAR Endocardial Generator over the set of ablation catheter electrodes.

Additional details are provided in the IFU LBL0774 for the specific use and procedural steps of the FARAWAVE Endocardial Ablation Catheter.

2.4.2 FARAFLEX Endocardial Ablation Catheter

The FARAFLEX Endocardial Ablation Catheter is a multi-electrode unidirectional, deflectable percutaneous catheter that connects to the FARASTAR Endocardial Generator and is designed to deliver PFA energy from the Endocardial Generator for cardiac tissue ablation. The FARAFLEX Endocardial Ablation Catheter is an adjunctive catheter designed to create smaller focal-type lesions for the following indications for use:

- Gap ablation to complete electrical isolation of the pulmonary veins,
- Focal ablation of cardiac arrhythmias, and
- Creation of ablation line between the inferior vena cava and the tricuspid valve.

The catheter consists of the following major sections: 1) distal section with electrodes arranged on four (4) splines, 2) catheter shaft, and 3) proximal handle with manually operated deflection and deployment controls, flush port, and connector. **Figure 4** depicts a deployed FARAFLEX Endocardial Ablation Catheter.

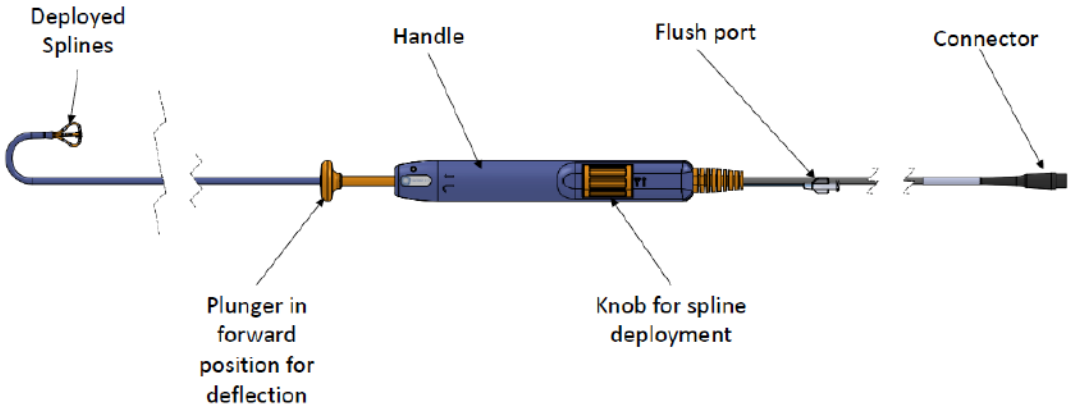

Figure 4. FARAFLEX Endocardial Ablation Catheter

The catheter can be deployed into basket-shaped configurations to accommodate various anatomical locations. The ablation catheter is visible under fluoroscopy due to the presence of marker bands at the distal tip and proximal end of the splines, as well as electrodes on each of four (4) splines.

2.4.3 FARASTAR Generator

The FARASTAR Generator consists of the following components – Pulsed Field Ablation Generator (PFAG), Stimulator Interface Box (SIB), SIB to Generator cable, Generator to Recording/Mapping System Pin box cable, and Recording Switch Box. The Endocardial Generator is designed to deliver PFA energy to endocardial sites in the heart via the FARAWAVE and FARAFLEX Endocardial Ablation Catheters (refer to IFU LBL0774 and IFU LBL0776 for the specific use and procedural steps of the Endocardial Ablation Catheters, respectively; LBL0771 for the FARADRIVE Steerable Sheath, LBL0193 for the FARADRIVE Deflectable Sheath, LBL0784 for the FARASTAR Generator, and LBL0892 for the Recording Switch Box).

The FARASTAR Endocardial Generator is a 12-channel output unit that generates a pulsed voltage waveform that can be delivered to the FARAWAVE or FARAFLEX ablation catheters. The user selectable voltage range for the FARAWAVE Ablation Catheter is 1800V to 2000V and the range for the FARAFLEX Ablation Catheter is 1200V to 1800V.

The FARASTAR Generator includes a two channel Cardiac Stimulator that can be connected to user supplied pacing catheters through the SIB. The FARASTAR energy delivery is synchronized with the Cardiac Stimulator outputs. The physician confirms pacing capture by actuating a button on the FARASTAR Endocardial Generator user interface prior to initiating energy delivery.

Details regarding the generator are provided in the FARASTAR Generator User Manual LBL0784.

2.4.4 FARADRIVE Deflectable and Steerable Sheaths

The FARAWAVE Endocardial Ablation Catheter and FARAFLEX Endocardial Ablation Catheter are used with either the FARADRIVE Deflectable Sheath or the FARADRIVE Steerable Sheath. The FARADRIVE Deflectable Sheath is the sheath used in the IMPULSE, PEFCAT, PEFCAT II, and PersAFOne clinical investigations studying the FARAPULSE Endocardial Ablation System and FARAPULSE Endocardial Multi Ablation System. The FARADRIVE Steerable Sheath is identical in design to the FARADRIVE Deflectable Sheath, except for cosmetic changes.

The FARADRIVE Deflectable Sheath consists of two (2) primary components: Steerable Sheath and Dilator, which are used together. Both components are sterile and single use only.

The FARADRIVE Deflectable Sheath is comprised of a distal deflectable section and a shaft section which connect to the handle. The handle includes a knob to control the deflection of the distal tip and a flush port for infusion of saline or contrast. The Dilator is intended for insertion through the sheath lumen and includes a shaped tip for dilation for vascular or chamber access (Figure **5**).

The FARADRIVE Steerable Sheath consists of two (2) primary components: Steerable Sheath and Dilator, which are used together. Both components are sterile and single use only.

The FARADRIVE Steerable Sheath is comprised of a distal deflectable section and a shaft section which connect to the handle. The handle includes a knob to control the deflection of the distal tip and a flush port for infusion of saline or contrast. The Dilator is intended for insertion through the sheath lumen and includes a shaped tip for dilation for vascular or chamber access (Figure **5**).

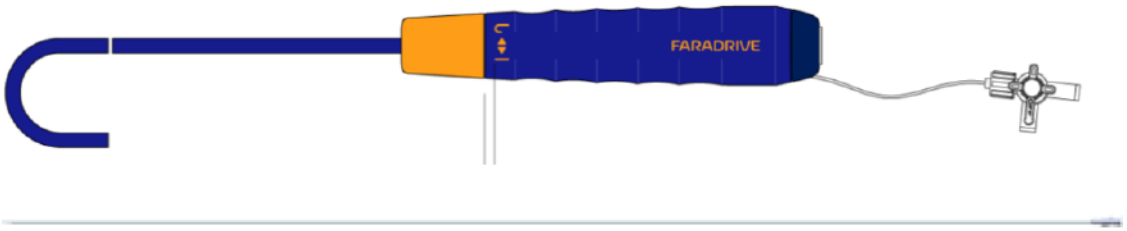

Figure 5. FARADRIVE Steerable Sheath and Dilator (equivalent to FARADRIVE Deflectable Sheath)

2.5 Device Accountability

The FARAPULSE Ablation System Plus will be stored in a secure location and access will be controlled. Records will be maintained to document the physical location of inventory from shipment and removal from Sponsor or Contract Manufacture facility through use and / or return or disposal.

The site will be responsible for maintaining a Device Accountability Log provided by the Sponsor or its designated representative. At a minimum the following will be recorded: Date of receipt, FARAPULSE Ablation System Plus components identification number (Generator, Ablation Catheter, Deflectable Sheath, and Steerable Sheath lot and / or serial number), expiration date, date of use, subject unique identification code and date of disposal or return of the device.

If there is a product Device Deficiency / Malfunction or other need to return the system or system components to the Sponsor or Contract Manufacture, the Sponsor or designee should be contacted for safe product disposal and/ or return details. Appropriate CRF will be completed in the event of a Device Deficiency / Malfunction.

The Investigator is responsible for ensuring that the investigational devices are used only under the Investigator's supervision and are only used according to this protocol and any approved amendments. The Investigator will not supply an investigational device to any person not authorized to participate in the study. The Investigator shall document on the Case Report Forms (CRFs) the lot numbers and / or serial numbers of the devices used during each case.

2.6 Return of Devices

All unused investigational devices will be returned to the Study Sponsor or designee upon completion of the clinical study. Any investigational device that does not meet performance specifications will also be returned to the Study Sponsor or designee for analysis per company procedures. The Investigator or his/ her designated representative is responsible for device accountability and disposition of all used and unused devices. The Study Sponsor or its designated representative will conduct device reconciliation at the completion of subject enrollment or at the conclusion of the study.

3. Study Design

3.1 Study Objective

The objective of this pilot study is to confirm that endocardial ablation using the FARAPULSE Ablation System Plus with commercial design devices is both safe and effective for treating drug-resistant paroxysmal atrial fibrillation (PAF).

3.2 Study Overview

This is a prospective, multi-center, single arm safety and effectiveness pilot study. Subjects will undergo percutaneous PFA ablation for pulmonary vein isolation and at the clinical discretion of the investigator receive PFA ablation of additional arrhythmogenic locations. Subjects will be followed at 7 days (telephonic), 30 days, 90 days, 6 months and 12 months for adverse events, recurrence of arrhythmia after a 90-day Blanking Period and other relevant outcome measures.

3.3 Subject Confidentiality

Enrolled subjects will be assigned a unique, pseudo-anonymous identifier that will be used to maintain confidentiality of each subject's medical information. Subject names and other protected health information will not be captured on the CRFs. In addition, all patient identifiers except the unique pseudo-anonymous identifier should be redacted from any images or other data submitted from the participating site to the Sponsor or the Sponsor's designated reviewers for analysis. All information concerning subjects or their participation in this study will be considered confidential. Only the authorized Sponsor, designated representative personnel, designated consultants and regulatory agencies will have access to these confidential files.

3.4 Written Informed Consent

All subjects must provide written Informed Consent using the EC-approved ICF before undergoing any study related procedures.

Routine clinical evaluations that would be performed as part of the normal clinical care of patients may be performed prior to such consent and used as part of the screening assessment. If the subject is subsequently consented and enrolled in the study, the results of such evaluations may be used as study data.

Subjects cannot be asked to sign the ICF until the study has been fully approved by the institution's EC and by the CA, if applicable, and the Sponsor or their CRO representative has received and reviewed the EC-approved ICF. Subjects who meet the general entry criteria will be asked to sign an ICF as approved by the relevant regulatory authorities before any study-specific tests or procedures are performed.

The Investigator or a designated member of his / her staff should approach the subject to obtain written informed consent. As far as possible, non-technical language shall be used that is understandable to the subject. The background of the proposed study and the benefits and risks of the procedures and study should be explained. The subject should be provided with ample time to read the ICF and discuss it with their family and physician. The subject shall be informed that his / her participation in the clinical investigation is confidential. The ICF must be read and understood by the subject and

the subject's questions answered. The ICF must be signed and dated by both the subject and Investigator conducting informed consent prior to subject enrollment and before the subject undergoes any study-related procedures. All subjects are to receive copies of their signed and dated ICF. A copy of the approved ICF along with a copy of each patient's signed ICF will be maintained by the Investigator in a designated clinical study administrative file. Subjects may not be consented after receiving any medication that might alter their ability to comprehend the consent form (e.g. sedatives, narcotics, etc.). Study personnel should explain that even if a subject agrees to participate in the study and signs the ICF, the subject may not be eligible to participate if he / she fails to meet the screening criteria.

Written informed consent must be obtained prior to performing any protocol driven tests or any procedures that are not standard of care for a percutaneous ablation procedure that the subject is scheduled to undergo.

Once written consent has been obtained, the subject will be entered on a Screening Log, which will be maintained at each site. All subjects who provide written informed consent will be entered on the screening log regardless of whether or not they are enrolled in the study.

3.5 Study Entry Criteria

3.5.1 Inclusion Criteria

Study subjects are required to meet all the following inclusion criteria to participate in this study:

1. Patients with documented drug resistant symptomatic PAF meeting all three of the following criteria:
   a. Confirmed AF: Documentation may include a recording such as ECG, transtelephonic monitor (TTM), Holter monitor, implanted devices, or telemetry strip, recorded within one year prior to enrollment and showing at least 30 seconds of AF.
   b. Frequent AF, defined as ≥ 2 episodes within 6 months of enrollment.
   c. Failed atrial fibrillation drug (AAD) treatment, meaning therapeutic failure of at least one AAD (class I – IV) for efficacy and / or intolerance.
2. Patients who are ≥ 18 and ≤ 75 years of age on the day of enrollment.
3. Patient participation requirements:
   a. Lives locally.
   b. Is willing and capable of providing Informed Consent to undergo study procedures.
   c. Is willing to participate in all examinations and follow-up visits and tests associated with this clinical study.

3.5.2 Exclusion Criteria

Subjects will be excluded from participating in this study if they meet any one of the following exclusion criteria:

1. Atrial fibrillation that is any of the following:
    a. Persistent (by diagnosis or continuous duration > 7 days)
    b. Secondary to electrolyte imbalance, thyroid disease, alcohol or other reversible / non-cardiac causes
    c. Requires ≥ 4 cardioversions in the preceding 12 months
2. Left atrial anteroposterior diameter ≥ 5.0 cm as documented by transthoracic echocardiography (TTE) or computed tomography (CT)
3. At any time, one or more of the following cardiac procedures, implants or conditions:
    a. Clinically significant arrhythmias other than AF, AFL or AT
    b. Any previous endocardial or epicardial ablation or surgery for AF
    c. Hemodynamically significant valvular disease
    d. Any prosthetic heart valve
    e. Heart failure – any of the following:
        i. NYHA Class III or IV CHF
        ii. LVEF <40%
        iii. Heart failure hospitalization
    f. Atrial or ventricular septal defect closure
    g. Atrial myxoma
    h. Left atrial thrombus
    i. Left atrial appendage device or occlusion
    j. Pacemaker, implantable cardioverter defibrillator or cardiac resynchronization therapy devices
    k. Significant or symptomatic hypotension
    l. Bradycardia or chronotropic incompetence
    m. History of pericarditis
    n. History of rheumatic fever
    o. History of congenital heart disease with any residual anatomic or conduction abnormality
    p. Any pulmonary vein abnormality, stenosis or stenting
4. Any of the following cardiovascular procedures, implants or conditions within the specified interval related to the date of enrollment:
    a. Within the 3 months preceding enrollment:
        i. Myocardial infarction
        ii. Unstable angina
        iii. Percutaneous coronary intervention
        iv. Treatment with amiodarone
    d. Within the 6 months preceding enrollment:
        i. Heart surgery
        ii. Stroke or TIA
        iii. Any thromboembolic event

iv. Carotid stenting or endarterectomy
v. Pericarditis or pericardial effusion

e. Within the 12 months following enrollment:
i. Any likelihood of cardiac surgery or transplant

5. History of blood clotting or bleeding abnormalities
6. Contraindication to, or unwillingness to use, systemic anticoagulation
7. Contraindications to both CT and MRI
8. Sensitivity to contrast media not controlled by premedication
9. Women of childbearing potential who are pregnant, lactating, not using birth control or planning to become pregnant during the anticipated study period
10. Medical conditions that would prevent participation in the study, interfere with assessment or therapy, significantly raise the risk of study participation, or confound data or its interpretation, including but not limited to:
    a. Body mass index (BMI) > 40
    b. Solid organ or hematologic transplant, or currently being evaluated for an organ transplant
    c. Severe lung disease, pulmonary hypertension, or any lung disease involving abnormal blood gases or significant dyspnea
    d. Renal insufficiency with an estimated creatinine clearance < 30 mL/min/1.73 m2, or any history of renal dialysis or renal transplant
    e. Active malignancy or history of treated cancer within 24 months of enrollment
    f. Clinically significant gastrointestinal problems involving the esophagus, stomach and/or untreated acid reflux
    g. Clinically significant infection
    h. Predicted life expectancy less than one year
11. Clinically significant psychological condition that in the investigator's opinion would prohibit the subject's ability to meet the protocol requirements.
12. Current or anticipated enrollment in any other clinical study

3.6 Enrollment

Subjects that meet all the eligibility criteria and are deemed suitable by the investigator will be invited to participate in the study.

Subjects will be considered enrolled at the time of signing the ICF.

Each subject will be assigned a unique study identification code to protect each subject's confidential health information. The unique study identification code will not include date of birth or subject's first and last initials and will be used to link study data and other study information to the subject in lieu of the subject name. The Subject Name Log will be used to link the unique study identity code to the subject and will be maintained at the site. This log will remain confidential and will not be provided to the Sponsor, but only used for reference when monitoring at the study site.

3.7 Sample Size

Up to 50 subjects with no more than 15 subjects being enrolled at any one site.

3.8 Investigational Sites

The clinical study will be conducted at up to six (6) European investigational sites.

3.9 Duration of Subject Participation

Site initiation and investigator training is estimated to take 3 months. The enrollment period is estimated to take 4 months and subjects will be followed for up to 13 months.

Procedural and 7-day data for regulatory submission should be available approximately 5 months after first enrollment.

The total study duration will be approximately 20 months from the beginning of site training to final study follow-up.

3.10 Subject Completion or Withdrawal

3.10.1 Study Completion

Once the subject has completed the final 12 month follow-up visit they are to be exited from the study. After study completion patients will return to standard medical care

3.10.2 Voluntary Withdrawal

Subjects may voluntarily withdraw from the study at any time for any reason.

3.10.3 Investigator Initiated withdrawal

The investigator may withdraw the subject due to any of the following situations:

- adverse event (AE); or
- study investigator may withdraw a patient from the study without the patient's consent if the investigator has a concern for the patient's rights, safety or welfare

3.10.4 Documentation

At the time of study withdrawal or completion for any reason, the study exit CRF will be completed, including the reason for exit.

3.10.5 Continuing Medical Care

Subjects leaving the study at any time will continue to receive appropriate medical care without prejudice.

3.10.6 Treatment of Pregnancies Identified During Subject Participation

If a subject becomes pregnant during participation in the study, the patient will be excluded from further study assessments and will return to standard medical care. These subjects will, however, continue to be followed for safety.

3.10.7 Lost to Follow-Up

If the investigator has attempted to contact a subject at least three times within 60 days and received no response, the subject may be considered lost to follow-up. The

investigator will document that a minimum of three attempts were made to contact the subject, including sending a certified letter if current address is known, prior to exiting the subject from the study.

At the time of confirmed lost to follow-up status, the study exit CRF will be completed.

3.11 Procedures

3.11.1 Index Procedure

The investigator will confirm that the following have been achieved:

- For women of childbearing potential – a negative pregnancy test
- Baseline NIHSS score
- The patient is not on amiodarone

FARAPULSE Endocardial Ablation procedure patients will undergo anesthesia according to institutional protocol. They will then be prepared in conventional sterile fashion for a cardiac catheterization procedure. Femoral vein access will be obtained via Seldinger technique. Transseptal access to the left atrium will then be obtained using a commercially approved sheath and Brockenbrough needle. The transseptal sheath will then be withdrawn, leaving guidewire access to the left atrium. The FARADRIVE Steerable Sheath or FARADRIVE Deflectable Sheath will then be prepared and advanced via guidewire to the left atrium. Commercially approved multielectrode pacing catheters will then be placed via conventional technique at the investigator's discretion. A baseline electrophysiological assessment of pulmonary vein connection to the left atrium will be made and documented via FARAWAVE or a commercially approved diagnostic catheter placed in each addressable pulmonary vein. A baseline 3D electroanatomical map may also be made at the investigator's discretion. The diagnostic catheter, if used, will then be removed from the FARADRIVE Steerable Sheath or FARADRIVE Deflectable Sheath.

The FARAWAVE Ablation Catheter will then be prepared and advanced over the guidewire to the left atrium through the sheath. The guidewire will be advanced into a target pulmonary vein, the catheter splines will be deployed to suit target anatomy by retracting the deployment knob, and the deployed catheter will be advanced to the ostium of the target pulmonary vein. At the investigator's discretion, contrast venography may be performed to verify placement of the catheter at the ostium. Cardiac pacing capture from the external cardiac stimulator will be obtained via connection to a diagnostic catheter. Once pacing capture is confirmed, ablation will be performed. Ablation dose will be selected at the investigator's discretion in accordance with LBL0784, FARASTAR Generator User Manual.

Ablation with the FARAWAVE Ablation Catheter may be repeated at the same site or at another target site at the physician's discretion using deployment configurations to suit target anatomy. Each addressable pulmonary vein will be ablated in turn beginning with placement of the guidewire, deployment of the ablation catheter, confirmation of pacing capture, and ablation. The effect of the ablation(s) may be checked post-procedure by pacing maneuvers, ECG recordings, 3D electroanatomic

mapping, or by using the mapping electrodes on the ablation catheter splines. Ablation using the FARAFLEX Ablation Catheter may be performed to close gaps in electrical isolation of pulmonary veins, focally ablate cardiac arrhythmias, or create a line of ablation at the cavo-tricuspid isthmus (CTI).

For a detailed description of procedure workflow refer to LBL0771 (FARADRIVE Steerable Sheath), LBL0193 (FARADRIVE Deflectable Sheath), LBL0774 (FARAWAVE Endocardial Ablation Catheter), LBL0776 (FARAFLEX Endocardial Ablation Catheter, LBL0784 (FARASTAR Generator), and LBL0892 (Recording Switch Box).

3.11.2 Reablation Procedure

Patients with recurrent AF, AFL or AT may undergo a second ablation procedure (reablation) with the experimental devices on or before the end of the Blanking Period (Day 90). This reablation procedure will follow the steps contained in **Section 3.11.1, Index Procedure**, as determined by investigator discretion to achieve protocol-required mapping and any required reablation.

3.11.3 Blanking Period

The Blanking Period consists of Day 0 (the date of Index Procedure) through and including Day 90.

During the Blanking Period, any recurrence of AF will be documented; however, recurrences of AF, AFL or AT during this time will not be considered Therapeutic Failures.

Subjects may undergo one repeat ablation during the Blanking Period without creating a Therapeutic Failure, following the procedure detailed in the preceding sections. This may occur during the Remap Procedure or at another procedure as clinically indicated.

If a second repeat ablation procedure is performed during this time, or any nonstudy device is used for cardiac ablation, the subjects will be considered a Therapeutic Failure but will remain in the study.

Towards the end of the Blanking Period, any AFD treatment will be discontinued unless the Investigator deems the withdrawal of AFD treatment not to be in the best interests of the patient.

3.11.4 Arrhythmia Core Lab

An Arrhythmia Core Lab (ACL) will oversee the provision, collection and analysis of data from the Event Monitors and Holter Monitors specified in this protocol.

- The subject will be instructed on the use of an Event Monitor at or before the Day 90 follow-up visit. Either ACL or the site will provide the subject with an Event Monitor not later than Day 90 to be used through the remainder of the 12-month follow-up interval for weekly scheduled and ad hoc symptomatic monitoring. The Event Monitor will be returned to the ACL or the site at the

time of the subject's exit from the study. ECG data from the Event Monitor will be analyzed by the ACL.

- The subject will be instructed on the use of a 24-hour continuous ECG (Holter) monitor prior to the 6-Month and if needed the 12-Month Holter monitoring. The ACL or the site will provide the subject with a Holter monitor within the specified window for the 6 and 12-Month Visits. The device will be worn by the subject for a single 24-hour period and then returned to the ACL or the site. ECG data from this monitor will be analyzed by the ACL.

3.12 Schedule of Events and Assessments

Subjects will complete the following visits and assessments as indicated below and as summarized in **Section 3.13 Table 3 Summary of Study Assessments**.

3.12.1 Baseline

Baseline data will be collected within 30 days of the date of enrollment unless otherwise specified. This data will include:

- Medical history
- AFD and anticoagulation medication history
- Pregnancy test (all women of child-bearing potential)
- 12-lead ECG
- Cardiac CT or MRI adequate to characterize left atrial and pulmonary vein dimensions
- TEE or other guideline-recommended imaging modality for exclusion of left atrial thrombus
- NYHA Classification
- NIHSS score
- CHA_2DS_2-VASc score
- EQ-5D-3 L quality of life assessment
- For Neurologic Assessment Subpopulation subjects: Cranial MRI

3.12.2 Index Procedure

The Index Procedure will be performed according to **Section 3.11.1, Index Procedure**. Procedural data will be collected including:

- Pregnancy test (all women of childbearing potential if baseline pregnancy test obtained more than 14 days prior to procedure)
- Post-ablation 3D electroanatomical maps
- Post-ablation fluoroscopic examination of diaphragm motion to assess phrenic nerve response
- Adverse Events
- Procedural times
- Lesion set data
- Device deficiencies and malfunctions

3.12.3 Pre-Discharge

Prior to hospital discharge the study data will be collected including:

- Adverse Events
- Data regarding the use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications.
- Cardiac rhythm as determined by a 12-lead ECG
- Occurrence, date, indication and outcome of any cardioversion(s)
- At the investigator's discretion: a post-procedural mediastinal gadolinium-enhanced MRI
- Stroke/TIA assessments
  - NIHSS score
  - A neurologic examination will be performed and recorded if:
    - If the NIHSS score has increased by 2 or more points
    - If there is a clinical suspicion of stroke or TIA
    - A post-procedure cranial MRI shows changes from a pre-procedure MRI (see Section 3.12.11, Neurologic Assessment Subpopulation)
- For Neurologic Assessment Subpopulation subjects: Cranial MRI
- Anticoagulation Monitoring:
  - For subjects on NOAC, perform a PTT and, at the investigator's discretion, a thrombin time
  - For subjects on warfarin, assessment of INR therapeutic levels

3.12.4 7-Day Telephone Assessment

Subjects will be contacted by telephone between Day 7 and 10 post-Index Procedure. Study data will be collected by interview, including:

- Adverse Events
- Symptoms of recurrent arrhythmia
- Data regarding the use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications.
- Cardioversions, ablations or hospital admissions since last visit

3.12.5 30-Day Visit

Discharged subjects will return for an office visit 30 days (± 7 days) post-ablation treatment. (Any subject who continues to be hospitalized 30 days post-ablation will have their 30-Day Visit assessment performed in-hospital). Study data will be collected including:

- Adverse Events
- Symptoms of recurrent arrhythmia
- Data regarding the use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications.
- Cardiac rhythm as determined by a 12-lead ECG at the time of the visit
- Cardioversions, ablations or hospital admissions since last visit

- Heart failure status as assessed by NYHA classification at the time of visit

3.12.6 Reablation Procedure

A study subject may undergo one reablation using the experimental devices without constituting a therapeutic failure if that reablation occurs on or before the end of blanking (day 90). In such cases, the following data will be collected:

- All data required for the Index Procedure will be gathered, utilizing the Reablation Procedure CRF pages.
- 3D electroanatomical remapping procedure will characterize the status of PVI for each vein, and each additional lesion type performed at the Index Procedure to characterize lesion durability.
- Any electrical gaps may be treated at the investigator's discretion using study devices, or if necessary, a commercially approved ablation device (which constitutes a Therapeutic Failure).
- For patients who received extra-PV ablation at index, including those receiving ablation of the CTI, the persistence of nonconductivity in targeted tissue will be evaluated with either pacing maneuvers or electroanatomical mapping.

Procedure-specific data will be collected including:

- Procedural times
- Lesion set data
- Device deficiencies and malfunctions

3.12.7 90-Day Visit

Subjects will return for an office visit at Day 90 ± 14 days following the Index Procedure.

Event Monitor Training: Within the 90 ± 14 day window for this visit, the subject will receive training regarding the use of, and the importance of, event monitoring. The event monitor shall be used for weekly scheduled and any symptomatic unscheduled monitoring throughout the remainder of study follow-up.

AFDs: In general, AFDs should be stopped before Day 104 (the end of the 90-Day visit window) to allow assessment of off-drug freedom from recurrent AF. However, AFDs may be continued if the investigator determines that this is in the subject's best interest.

Study data will be collected at the 90-Day Visit including:

- Adverse Events
- Symptoms of recurrent arrhythmia
- If either the post-Index Procedure or Reablation Procedure fluoroscopies indicated diminished phrenic nerve response, and resolution has not been previously demonstrated, a repeat fluoroscopic examination
- Data regarding the use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications
- Cardiac rhythm as determined by a 12-lead ECG at the time of the visit
- Cardiac CT or MRI scan to assess the patency of the pulmonary veins
- Cardioversions, ablations or hospital admissions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Anticoagulation Monitoring:
    - For subjects on NOAC, perform a PTT and, at the investigator's discretion, a thrombin time
    - For subjects on warfarin, assessment of INR therapeutic levels

3.12.8 6-Month Visit

Subjects will return for an office visit 6 months (180 days ± 30 days) following the Index Procedure.

Holter Monitor Training: Within the 180 ± 30 day window for this visit, this visit, the subject will receive training regarding the use of, and the importance of, 24 hour continuous ECG monitoring. The Holter Monitor will be used for a 24 hour monitoring within the visit window.

Event Monitor Compliance: Within the 180 ± 30 day window for this visit, and preferably at the visit, Event Monitor compliance will be reviewed for weekly scheduled and ad hoc symptomatic monitoring and retraining of the subject provided as needed.

Study data will be collected at the 6-Month Visit including:

- Adverse Events
- Symptoms of recurrent arrhythmia
- If either the post-Index Procedure or Reablation Procedure fluoroscopies indicated diminished phrenic nerve response, and resolution has not been previously demonstrated, a repeat fluoroscopic examination
- Data regarding the use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications
- Cardiac rhythm as determined by a 12-lead ECG at the time of the visit
- Cardioversions, ablations or hospital admissions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Anticoagulation Monitoring:
  - For subjects on NOAC, perform a PTT and, at the investigator's discretion, a thrombin time
  - For subjects on warfarin, assessment of INR therapeutic levels

3.12.9 12-Month Visit

Subjects will return for an office visit 12 months (365 days ± 30 days) following the Index Procedure. During this visit, the subject will receive training regarding the use of, and the importance of, 24 hour continuous ECG monitoring.

Holter Monitor Training: Within the 365 days ± 30 day window for this visit, this visit, the subject will receive training regarding the use of, and the importance of, 24 hour continuous ECG monitoring. The Holter Monitor will be used for a 24 hour monitoring within the visit window.

Study data will be collected at the 12-Month Visit including:

- Adverse Events
- Symptoms of recurrent arrhythmia
- If either the post-Index Procedure or Reablation Procedure fluoroscopies indicated diminished phrenic nerve response, and resolution has not been previously demonstrated, a repeat fluoroscopic examination
- Data regarding the use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications.
- Cardiac rhythm as determined by a 12-lead ECG at the time of the visit
- Cardioversions, ablations or hospital admissions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- EQ-5D-3 L quality of life assessment
- Anticoagulation Monitoring:
  - For subjects on NOAC, perform a PTT and, at the investigator's discretion, a thrombin time
  - For subjects on warfarin, assessment of INR therapeutic levels

3.12.10 Unscheduled Visits

Any unscheduled follow-up visits that occur throughout the study, other than routine follow-up visits per the institution's or investigator's normal standard of care, shall be documented. Study data will be collected including:

- Adverse Events
- Symptoms of recurrent arrhythmia
- Cardiac rhythm as determined by a 12-lead ECG at the time of the visit
- Event Monitor compliance will be reviewed for weekly scheduled and ad hoc symptomatic monitoring and retraining of the subject provided as needed.
- Cardioversions, ablations or hospital admissions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Anticoagulation Monitoring:
    - For subjects on NOAC, perform a PTT and, at the investigator's discretion, a thrombin time
    - For subjects on warfarin, assessment of INR therapeutic levels

3.12.11 Neurologic Assessment Subpopulation

An investigator may elect to have a series of study subjects undergo pre- and post-ablation cranial MRIs to assess the occurrence of subclinical emboli (SCE) during the Index Procedure. The post-ablation MRI will be obtained between 24 and 72 hours following the conclusion of the ablation procedure.

3.13 Schedule of Study Assessments

Table 3. Summary of Study Assessments

Assessment	Baseline	Procedure	Pre-Discharge	7-Day Call	30-Days Post-Procedure (± 7 days)	Reablation Procedure (if required)	90-Day Follow-up (90 ± 14 days)	6-Month (180 ± 30 days)	12-Month (365 ± 30 days)	Unscheduled
Medical History, CHA_2DS_2-VASc	X									
AFD and Anticoagulant Medications	X		X	X	X	X	X	X	X	X
Symptoms of recurrent arrhythmia				X	X	X	X	X	X	X
History of cardioversions, ablations, hospital admissions since last visit			X	X	X	X	X	X	X	X
Pregnancy test (for females of childbearing potential)	X	X				X				
12-lead ECG	X		X		X	X	X	X	X	X
24-Hour Continuous ECG Monitor (e.g., Holter)								X	X	
Cardiac CT/MRI for LA and PV dimensions	X					X				
Mediastinal MRI			X[1]							
TEE or other imaging modality (to exclude left atrial thrombus)	X									
Electroanatomical Mapping		X				X				
Event Monitor readiness/compliance						X	X	X	X	X
NIHSS	X		X							
Neurologic exam			X[2]							
Cranial MRI	X[3]		X[3]							
NYHA Classification	X		X		X	X	X	X	X	X
Fluoroscopic Examination of Diaphragm		X				X	X[4]	X[4]	X[4]	
Anticoagulation Monitoring			X[5]		X[5]	X[5]	X[5]	X[5]	X[5]	X[5]
EQ-5D-3 L QoL assessment	X								X	
Adverse Events		X	X	X	X	X	X	X	X	X

[1] At investigator's discretion
[2] If NIHSS score has increased by 2 or more points or if clinical suspicion of stroke/TIA
[3] In Neurologic Assessment Subpopulation only
[4] If the Index Procedure or Remap Procedure study indicated decreased phrenic nerve function and resolution has not yet been demonstrated.
[5] INR or PTT (as applicable for patient on heparin or NOACs); ACT for procedural monitoring

4. Benefit Risk Assessment

The Sponsor has conducted an analysis of the benefits and risks of the FARAPULSE Ablation System Plus and ablation procedure as described below. The conclusion of this review is that the subject investigation is justified because the overall potential benefit to the population outweighs the risks.

4.1 Potential Adverse Events

The following anticipated adverse events have been identified as possible complications of percutaneous atrial fibrillation ablation procedures in general as well as with the FARAPULSE Ablation System Plus:

- Access site complications (e.g., hematoma, pseudo-aneurysm, laceration, bleeding) potentially requiring surgical intervention
- Air embolism
- Allergic reaction or fever resulting from contact with catheters
- Anemia
- Arrhythmia, potentially requiring cardioversion, defibrillation, or rhythm management device
- Arteriovenous fistulae
- Back pain
- Bed sores
- Bleeding, hematoma, hemorrhage or aneurysm at vascular access sites
- Blood pressure changes including hypotension or hypertension
- Coronary artery or vein injury
- Cardiac tamponade or perforation
- Cardiac arrest or cardiac failure
- Catheter entrapment
- Cardiogenic shock
- Conduction system injury resulting in sinus arrest or heart block, either transient or permanent, potentially requiring pacemaker insertion
- Congestive heart failure
- Death
- Drug allergic reaction or side effects (e.g., from contrast, steroids, analgesics, anesthetics, anticoagulants, sedatives, etc.)
- Embolism due to presence of thrombus or introduction of air
- Esophageal injury, ulcer or fistula
- Hemorrhage
- Hemodynamic compromise
- Hemopericardium
- Hemoperitoneum
- Hemothorax
- Local infection, systemic infection, and/or sepsis
- Muscle contractions due to electric stimulation
- Myocardial infarction / transient ischemia

- Nerve damage
- Organ failure
- Pain
- Perforation (e.g., of diaphragm, liver, lung, and/or vessels).
- Pericardial irritation
- Pericardial effusion
- Pericarditis
- Peritonitis
- Phrenic nerve injury with paralysis of the diaphragm and breathing impairment
- Pneumomediastinum
- Pneumopericardium
- Pneumoperitoneum
- Pneumothorax
- Pulmonary vein injury or stenosis
- Risk of cancer or birth defect/harm to fetus from x-ray exposure
- Skin burns/irritation from x-ray exposure
- Stroke/transient ischemic attack
- Surgical procedure to remove retained catheter
- Thrombosis
- Vessel damage, dissection, or occlusion.

4.2 Potential Risks

As detailed in **Section 1.3, Summary of FARAPULSE Clinical Studies,** the risk profile associated with the FARAPULSE Ablation System Plus and the ablation procedure is expected to be consistent with similar devices currently in clinical use for percutaneous cardiac ablation for treatment of paroxysmal atrial fibrillation.

The FARAPULSE Ablation System Plus is a Pulsed Field Ablation (PFA) ablation system that produces continuous transmural cardiac lesions to treat atrial fibrillation using an ablation procedure that is similar to other commercially available percutaneous ablation catheters. More specifically:

- The device system is used during percutaneous endocardial ablation procedures like other commercially approved catheter systems.
- The device system is composed of similar biocompatible materials.
- The device system is a non-thermal ablation technology with targeted cardiac tissue specific mechanism of ablation.
- The device uses the standard percutaneous techniques for ablation procedures.
- The device utilizes a standard irreversible electroporation generator to deliver energy in the form of ablation dose.

A fundamental difference between the FARAPULSE Ablation System Plus and other commercially approved atrial fibrillation ablation systems is that the Pulsed Field Ablation or irreversible electroporation energy is delivered through electrodes

embedded in the endocardial ablation catheter for delivery of such energy in the pulmonary veins.

As such, the potential risks are roughly equivalent to those associated with commercially released systems being used for percutaneous cardiac ablation procedures. Currently, the complication rates for commercially available catheters are low and have declined as physicians have continued to learn more about cardiac ablation techniques. Furthermore, FARAPULSE, Inc. has conducted bench and in-vivo testing to ensure safe use of the device during clinical investigation and is in compliance with the applicable requirements of the Medical Device Directive 93/42/EEC.

4.3 Potential Benefits

There are no *guaranteed* benefits from participation in this study. Information gained from the conduct of this study may also be of benefit to other persons with the same medical condition.

This study of up to 50 patients will have the following potential benefits:

- To provide treatment to subjects with PAF using an investigational device which has demonstrated the ability to isolate pulmonary veins and reduce the subsequent occurrence of symptomatic atrial fibrillation in a small number of patients;
- To generate additional data demonstrating that the endocardial creation of electrically isolating lesions via Pulsed Field Ablation (PFA) catheter ablation applied using the FARAPULSE Endocardial Ablation System is a safe and potentially effective treatment for drug-resistant, recurrent, symptomatic paroxysmal atrial fibrillation (PAF);
- To assess the safety and effectiveness of the FARAFLEX Ablation Catheter for focal ablation in accordance with its proposed indication for use;
- To assess the protocol elements and design for subsequent use in a global multi-center pivotal trial.

5. Statistical Analysis and Reporting

A Statistical Analysis Plan (SAP) will be prepared that governs the collection, analysis and reporting of the data from this investigation. This section summarizes the essential elements of that plan.

5.1 General Statistical Considerations

All statistical analyses will be performed using validated statistical software. Continuous variables will be summarized using standard quantitative statistics: number of available observations, mean, standard deviation, median, quartiles and range (minimum and maximum observed values). The number of missing observations will also be specified.

Categorical variables will be summarized using classical frequency statistics: number of available observations and percentages by categories. Percentages will be calculated on the number of available observations. The number of missing observations will also be specified.

When applicable, bilateral asymptotic or exact confidence intervals for binomial distributions will be calculated at the 95% level.

A full data listing will be prepared. Data will be pooled from all study sites.

All related and resulting reports, documents and data will be produced and maintained in such a way as to ensure their control and the protection of subject privacy as far as is reasonably practicable. Data files and analytic reports will be archived according to requisite regulatory standards.

5.2 Control of Systematic Error and Bias

Subjects are not randomized in this single arm study and therefore masking is not achievable. Error and bias are being controlled by several means, including a comprehensive set of study procedures as defined in the protocol to ensure consistent management and outcome measure assessment. Follow-up Holter monitoring and event monitoring data, and all MRI/CT dimensions of PVs, will be assessed objectively by third parties according to standard clinical protocols. Primary effectiveness and safety outcomes will be reviewed by an independent Clinical Events – Data Monitoring Committee (CEDMC). A complete Study Report will allow scientific and clinical reviewers to independently assess potential error and bias.

Study outcomes will be reviewed and adjudicated by an independent Clinical Events and Data Monitoring Committee (CEDMC) more fully described in **Section 9.10, Clinical Events and Data Monitoring Committee.**

5.3 Sample Size Justification

This investigation is the next in a progressive series assessing the performance of the FARAPULSE Ablation System Plus. This is a pilot study with no formal hypothesis testing and therefore no required sample size. Study results will be

presented using descriptive statistics. Results from this study will be used to inform and design additional clinical studies.

50 subjects with a targeted enrollment of at least 30 at new sites who have not performed PFA before, utilizing the updated commercial design investigative devices allows assessment of the revised devices, confirms trial parameters and provides feedback on the training and oversight of new investigators.

5.4 Subject Disposition

The disposition of all subjects enrolled in the study will be described in tables and diagrams, including numbers screened, treated and assessed at each scheduled follow-up interval. Roll-in subjects will be assessed separately as part of the learning curve analysis. Subjects who do not complete the study will be enumerated and the reason(s) for their discontinuation will be described.

5.5 Imputation for Missing Data

Imputations for missing data in (e.g., withdrawn subjects, loss to follow-up, missing data) will not be performed. Analyses will be performed with all available data only.

5.6 Populations for Analysis

Enrolled Population: all subjects who provide their informed consent.

Safety Subjects: all enrolled subjects who begin the Index Procedure.

Intent to Treat Subjects: all safety subjects who undergo one or more ablations at the Index Procedure using the study device.

Per Protocol Subjects: Intent-to-treat subjects for whom the Index Procedure is completed without interfering investigational device deficiency or malfunction and who do not receive any ablations using a nonstudy device.

Roll In Subjects: Up to the first 2 intent-to-treat subjects per investigational site for whom the Index Procedure is completed without interfering investigational device deficiency or malfunction and who do not receive any ablations using a nonstudy device. Safety and effectiveness results for these patients will be fully reported, but not included in effectiveness endpoint calculations.

Reasons for exclusion from the populations will be given, and a summary of adverse events for these subjects, if any, will be provided.

5.7 Final Clinical Report

A final clinical report including these analyses will be prepared at the conclusion of the study or at such time as the study may be prematurely terminated. Copies of the final report will be provided to the investigator and their EC and to the CA as applicable.

6. Outcome Measures

6.1 Primary Safety Endpoint

The primary safety endpoint for this study is the Composite Safety Endpoint (CSE) defined as the incidence of the following serious adverse events (SAEs) which are device- or procedure-related, as adjudicated by the CEDMC based on the definitions contained in the Composite Safety Endpoint Definitions Table.

Early onset (within 7 days of an index or protocol-specified reablation procedure)

- Death
- Myocardial infarction
- Persistent diaphragmatic paralysis
- Stroke
- Transient ischemic attack
- Peripheral or organ thromboembolism
- Pericardial effusion, hemorrhage or tamponade
- Vascular access complications
- Hospitalization
- Heart block

Late onset (any time during follow-up)

- Pulmonary vein stenosis
- Atrio-esophageal fistula

* Excludes hospitalization (initial or prolonged) due to arrhythmia (AF/Atrial Flutter/Atrial Tachycardia) recurrence or due to non-emergent cardioversion (pharmacological or electrical). Excludes visits to hospital-associated outpatient facilities such as clinics or emergency wards.

Table 4. Composite Safety Endpoint Definitions

Adverse Event	Description/Criteria
Death	Death
Myocardial infarction*	Clinical evidence of acute myocardial ischemia with detection of a rise and/or fall of cTn (cardiac troponin) values with at least 1 value above the 99th percentile URL (upper reference limit) and at least one of the following: • Symptoms of myocardial ischemia • New ischemic ECG changes • Development of pathological Q waves • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology • Identification of a coronary thrombus by angiography or autopsy

Adverse Event	Description/Criteria
Persistent diaphragmatic paralysis	Diaphragmatic paralysis: Change from baseline in the elevation of a hemidiaphragm as demonstrated radiographically (chest X-ray or fluoroscopy) by elevation of the diaphragm above the normal range but not due to a pulmonary process such as atelectasis or pleural disease. Persistent: not resolved by completion of last study follow-up visit.
Stroke	An acute symptomatic episode of neurological dysfunction attributed to a vascular cause (ischemia or hemorrhage) in which symptoms last more than 24 hours, or if symptoms last less than 24 hours, a brain imaging study demonstrates infarction.
Transient ischemic attack	An acute episode of temporary (<24 hours) and focal loss of cerebral function of vascular (occlusive) origin.
Peripheral or organ thromboembolism	A cardiac thrombus that occludes a more distal arterial site. Cutaneous petechiae are excluded from this definition.
Pericardial effusion, hemorrhage or tamponade	The development of a significant pericardial hemorrhage, effusion or tamponade within 7 days of undergoing a protocol-specified ablation/reablation procedure. Significant: an event that results in hemodynamic compromise (e.g. systolic BP < 80 mm Hg) or requires pericardiocentesis or surgical drainage.
Vascular access complications	Vascular access complication (e.g. groin hematoma, AV fistula, pseudoaneurysm) requiring significant intervention (e.g. surgical repair, blood transfusion or thrombin injection).
Hospitalization	Includes any hospitalization, or prolongation of an existing hospitalization, for a related adverse event. Excludes a hospitalization which is necessitated solely due to: 1. The recurrence of arrhythmia (AF/atrial flutter/atrial tachycardia) recurrence, 2. Non-urgent cardioversion (pharmacological or electrical), or 3. A diagnostic procedure.
Heart block	Impairment of AV conduction that is related to a protocol-specified cardiac ablation procedure and which requires permanent pacing.
Pulmonary vein (PV) stenosis	>70% diameter reduction of pulmonary vein from baseline CT/MRA scan.
Atrio-esophageal fistula	Demonstration of a fistulous connection between the atrium and the lumen of the esophagus by radiographic, endoscopic or postmortem examination

* Thygesen et al, Fourth universal definition of myocardial infarction, Circulation, November 2018, accessed online at https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000000617 on July 31, 2019.

6.2 Additional Safety Analyses

The proportion of subjects:

1. With any adverse event in the Composite Safety Endpoint definitions table, whether or not adjudicated as an SAE
2. With a device- or procedure-related SAE
3. With a device- or procedure-related stroke or TIA
4. With a pre-post cranial MRI change (brain imaging subpopulation)
5. Requiring cardioversion
6. Requiring an arrhythmia-related hospitalization

Learning curve analysis.

6.3 Primary Effectiveness Endpoint

The proportion of subjects with:

- Acute Procedural Success, AND
- Therapeutic Success, defined as freedom from:
    - Post blanking period through assessment: occurrence of AF, AFL or AT, or ablation for AF/AFL/AT using the study device
    - At any time: ablation for AF/AFL/AT with a nonstudy device

Therapeutic success will be assessed between Day 91 and the 12 month ± 4 week follow-up visit.

6.4 Additional Effectiveness Analyses

1. Acute Procedural Success, defined as the percutaneous endocardial creation of an electrically isolating set of lesions around the ostia of pulmonary veins (PV) during the index procedure, as clinically assessed by entrance and/or exit block performed ≥ 20 minutes after the last PVI lesion is made on a per patient basis.
2. The primary effectiveness endpoint for subjects not on AFDs between Day 105 and the 12 month follow-up visit.
3. First pass isolation (index procedure) consisting of Acute Procedural Success after a single planned set of lesions in each attempted PV
4. The proportion of subjects with early recurrence of atrial fibrillation (ERAF) by 90 days after the initial study ablation
5. The proportion of attempted subjects that achieve Acute CTI Success, defined as the creation of bi-directional electrical block across the cavo-tricuspid isthmus using the investigational devices.
6. Learning curve analysis
7. Rate of any reablation through 12 months of follow-up

6.5 Procedural Assessments

1. Assessments of duration for procedure components
    a. Procedure time (initiation of venous access to venous access closure)
    b. Dwell time (sum of catheter entry-to-exit durations)
    c. Total ablation time (first ablation to last ablation)
    d. Fluoroscopy time (total duration of exposure)

2. Characterization of lesion sets:
    a. PVI ablations
    b. Extra-PV ablations, excluding CTI ablations
    c. CTI ablations
    d. Anomalous PV ablations

7. Adverse Events, Device Effects, Malfunctions and Deficiencies

7.1 Adverse Events

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 investigational medical device.

NOTE 1: This definition includes events related to the investigational medical device or the comparator.
NOTE 2: This definition includes events related to the procedures involved.
NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.
NOTE 4: This definition excludes medical conditions, findings or abnormalities present at the time of enrollment, which are defined as pre-existing conditions. Pre-existing conditions will not be included in the adverse event dataset. However, a worsening of a pre-existing condition during the study does constitute an adverse event.

7.2 Serious Adverse Events

A Serious Adverse Event (SAE) is an adverse event that led to:

- Death,
- Serious deterioration in the health of the subject, that either resulted in:
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - in-patient or prolonged hospitalization, or
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
- Fetal distress, fetal death or a congenital abnormality or birth defect.

NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
NOTE 2: "Life-threatening" means that the study subject was at a substantial and immediate risk of dying due to that adverse event as it occurred. "Life threatening" adverse events do not include an adverse event that had it occurred in a more severe form, might have caused death.
NOTE 3: "Hospitalization" is a physician-ordered inpatient hospital stay from one calendar day to the next or longer. Hospitalization does not include an outpatient facility visit or ER visit.
NOTE 4: The "prolongation" is related to the adverse event, excludes delays waiting for diagnostic results, is medically necessary and extends the hospital stay by at least one calendar day.
NOTE 5: "Impairment" is defined as a substantial disruption of a person's ability to conduct normal life functions.
NOTE 6: "Medical or surgical intervention" indicates a procedure or therapy with significant novel risk, delay or subject discomfort, that results from the adverse event. "Medical or surgical intervention" does not include oral medication, noninvasive diagnostic testing or blood testing, routine intravenous fluids or the administration of antibiotics.

7.3 Device Effects

7.3.1 Adverse Device Effects

An Adverse Device Effect (ADE) is an adverse event related to the use of an investigational medical device

NOTE 1: 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.
NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
NOTE 3: "Related to the uses of an investigational medical device" shall be defined for this protocol as a determination that the effects were probably or definitely related to an investigational device.

7.3.2 Serious Adverse Device Effects

A Serious Adverse Device Effect (SADE) is an adverse device effect (ADE) that has resulted in any of the consequences characteristic of a Serious Adverse Event. (SAE).

7.3.3 Unanticipated Serious Adverse Device Effects

An Unanticipated Serious Adverse Device Effect (USADE) is 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 as embodied in Section 4.1 of this CIP.

NOTE 1: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.
NOTE 2: If an SAE is determined to be probably or definitely related to the device and has not been previously anticipated, the clinical finding would be classified as an unanticipated serious adverse device effect (USADE).

7.4 Device Deficiencies

A Device Deficiency is an inadequacy of an investigational medical device related to its identity, quality, durability, reliability, safety or performance. This may include malfunctions, use error, or inadequacy in the information supplied by the manufacturer.

7.5 Use Errors

A "Use Error" is an act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user

NOTE 1: Use error includes slips, lapses, and mistakes.
NOTE 2: An unexpected physiological response of the subject does not in itself constitute a use error.

7.6 Malfunctions

A Malfunction is a failure of an investigational medical device to perform in accordance with its design specifications and intended purpose when used in accordance with the instructions for use or the subject CIP.

7.7 Causality Relationship

The investigator will assess the causality of all adverse events in relation to the investigational device or any other study-related procedures according to five different levels of causality:

1) Not related: relationship to the device or procedures can be excluded when:

- the event is not a known side effect of the product category the device belongs to or of similar devices and procedures;
- the event has no temporal relationship with the use of the investigational device or the procedures;
- the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
- the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;
- the event involves a body-site or an organ not expected to be affected by the device or procedure;
- the serious event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
- harms to the subject are not clearly due to use error;
- In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

2) Unlikely: the relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.

3) Possible: the relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.

4) Probable: the relationship with the use of the investigational device seems relevant and/or the event cannot reasonably have explained by another cause, but additional information may be obtained.

5) Causal relationship: the serious event is associated with the investigational device or with procedures beyond reasonable doubt when:

- the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
- the event has a temporal relationship with investigational device use/application or procedures;
- the event involves a body-site or organ that
- the investigational device or procedures are applied to;
- the investigational device or procedures have an effect on;
- the serious event follows a known response pattern to the medical device (if the response pattern is previously known);
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible);
- other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
- harm to the subject is due to error in use;
- In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

For the determination of device and procedure relatedness for this trial's safety outcome measures, causal and probable relationships will be deemed "related" and not related, unlikely and possible relationships will be deemed "unrelated." An analysis of adverse event categories by all five types of relationships will also be performed.

7.8 Reporting

AEs and SAEs:

All AEs, including all SAEs, will be monitored from the time of enrollment through discharge for this study. All AEs must be documented in the patient chart and recorded in the appropriate CRF or eCRF. A description of the event, including the start date, resolution date, action taken and the outcome shall be provided along with the Investigator's assessment of the seriousness of the event and the relationship between the AE and the study devices and/or procedures.

All AEs should be followed until the event is resolved, judged to be chronically stable or 12 month study follow-up has been completed. The investigational site will provide relevant follow-up information to the Sponsor or designee upon request.

The investigator shall also report to the Sponsor or its designee any Device Deficiencies or Malfunctions that did not but might have led to a SAE if such an event were to recur.

The investigator shall notify the Sponsor and the designated CRO immediately and **not later than 24 hours** after the Investigator has become aware of a **SAE or Device Deficiency / Malfunction that might have led to a SAE.**

The Investigator shall report the SAE or Device Deficiency / Malfunction on the appropriate CRF

Should mail correspondence be necessary, documents can be sent to the following:

CRO: MedPass International SAS
Fax: +33 (0)1 40 53 81 11

Sponsor: FARAPULSE, Inc.
Email: clinical@farapulse.com
Contact: Mr. Christopher Schneider

Return of Subject Device:

In all cases, and whenever possible the device involved in the AE, SAE, Device Deficiency / Malfunction as described above is to be returned to the Sponsor or Sponsor's designee for analysis and investigation, as appropriate. The Study Coordinator shall contact the Sponsor for instructions on returning the device.

Device Deficiencies and Malfunctions:

All Device Deficiencies / Malfunctions that did not contribute and would not likely contribute to a SAE, shall be documented on the Device Deficiency / Malfunction CRF and submitted to the Sponsor **within 7 days** after the observed Device Deficiency / Malfunction. The Sponsor's Quality Assurance function shall ensure an assessment is completed for each reported Device Deficiency / Malfunction. Such information shall be provided in the final clinical report.

Depending on the local requirements or following agreement between both parties, the Sponsor, its designated representative (CRO) or the Principal Investigator will be responsible for performing safety reporting to the Ethics Committee according to the relevant local regulatory requirements.

The Sponsor or designated representative (CRO) will be responsible for reporting to the National Competent Authority according to national requirements in accordance with MEDDEV 2.7/3.

8. Monitoring

Clinical monitors, qualified by training and experience, will be responsible for monitoring and overseeing the conduct of the study in accordance with the Study Monitoring Plan.

The clinical monitors will evaluate compliance with the protocol, any specific recommendations made by the site's EC and the signed Investigator Agreement. Phone contacts and site visits will be conducted to ensure that the protocol is being followed and that any protocol deviations are properly documented. Clinical monitoring will include a verification that the ICF was properly obtained for all enrolled study participants, a review of clinical records for accuracy and completeness, resolution of missing or inconsistent results and a review of source documents. The clinical monitor will verify that the CRFs agree with the source documentation and other records. The Investigator will make available to the clinical monitor for review all ICFs, all completed CRFs, source documentation and other relevant records for all enrolled subjects at the site.

If a deficiency is noted during an on-site monitoring visit or at any other time during the study, the clinical monitor is required to discuss the situation with the Investigator and the Sponsor to ensure compliance.

The Sponsor or its designated representative, qualified by training and experience, will be responsible for monitoring and overseeing the conduct of the study. The accuracy of all collected data will be verified for:

- Eligibility criteria
- Baseline characteristics
- Primary safety and feasibility endpoints
- Secondary endpoints
- Adverse events (including SAEs) and Device Deficiencies / Malfunction Reporting

Verification will utilize source documents including, but not limited to, medical records, office/ clinic notes, procedure reports, laboratory results, physician and nursing progress notes. Verification and quality of data, monitoring of clinical study progress and Investigator compliance with the approved protocol will be conducted by the Sponsor or its designated representative.

The Sponsor or its designated representative must be allowed to visit the clinical site and have direct access to all study records throughout the duration of the study. The monitor will review all source data and compare them to the data documented in the CRFs, in addition to performing a review of the Regulatory Site Binder and assessing device accountability. The Investigator and / or institution will provide direct access to source data/ documents for study-related monitoring, audits, and regulatory review and inspection.

It is important that the Investigator and other relevant site personnel, including the research study coordinator, are available for consultation with the clinical monitors

during the monitoring visits and that sufficient time is devoted at the site for the monitoring process.

Additionally, telephone, email contact, and onsite visits will be conducted on a regular basis with the Investigator and the site staff to ensure that the protocol is being followed and to address any issues that may occur during the study.

If a deficiency is noted during the study, the clinical monitor is required to discuss the situation with the site and the Sponsor (if required) to secure compliance. A Monitoring Site Visit Report will be issued to the Investigator and Sponsor.

9. Study Management

The Sponsor has overall responsibility for the conduct of the study according to Good Clinical Practice Guidelines (ICH E6 Consolidated Guidance to Good Clinical Practice) as well as any conditions imposed by local and national regulatory authorities.

For the subject investigation, the Sponsor will have direct responsibilities and will delegate other responsibilities to appropriate and qualified consultants, contractors and/ or CROs. Together, the Sponsor, consultants and CRO will ensure that the study is conducted according to the approved CIP, EC-approved ICF and all applicable governing regulations. All personnel to participate in the conduct of this clinical study will be qualified by education and/or experience to perform their tasks.

9.1 Key Contributors

9.1.1 Study Sponsor

FARAPULSE, Inc.
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9.1.2 CRO

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9.1.3 Arrhythmia Core Lab

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Czech Republic
Contact: Veronika Bolkova
Tel: +420 725 069 195
iowa@mdtekg.cz

9.2 Ethical Considerations

It is expected that all parties will share in the responsibility for ethical conduct in accordance with their respective roles in the investigation. The Sponsor and the Investigator shall avoid improper influence or inducement of the subject, monitor, other clinical investigator or other parties participating in or contributing to the clinical investigation.

9.2.1 Study Conduct

The study will be performed in accordance with the relevant parts of the Code of Federal Regulations, ICH Guidelines for Good Clinical Practices, the European Standard ISO 14155, the Declaration of Helsinki, and any regional and/or national regulations. The clinical investigation shall not begin until the required approval has been obtained from the National CA and the local EC. Any additional requirements imposed by the regulatory authority or EC shall be followed. These principles shall prevail over interests of science and society and shall be understood, observed and applied at every step in this clinical investigation.

9.2.2 Ethics Review

Before any subject can be enrolled in this study, the local or national EC and the CA must review and approve the CIP and the ICF to be used. A subject cannot be asked to sign the ICF until the study has been fully approved by the institution's EC and by the CA, if applicable. The Sponsor or their designated CRO will require a copy of any EC correspondence, as well as the final EC approval letter and the final EC-approved ICF, and approvals for the CIP and ICF revisions on amendments from the EC. The Sponsor or their designated CRO will keep all the CA correspondence, as well as the CA approval letter.

9.2.3 Informed Consent

Subjects will not sign the ICF until the study has been fully approved by the institution's Ethics Committee and the Sponsor or their designated CRO has received and reviewed the specific EC-approved ICF. When the Investigator has determined the eligibility of a specific subject to enter the study, the ICF must be completed. The ICF must be read and understood by the subject, the subject's questions answered, and the form signed by the subject before any study-related procedures can be performed. All subjects are to receive copies of their signed ICF.

9.2.4 Coverage of Expenses

Study participants will be reimbursed for travel costs related to study hospital visits.

9.2.5 Sharing New Information

If new information becomes available that can significantly affect a subject's future health and medical care,that information shall be provided to the subject(s) affected in written form by the investigator. The sponsor will provide all such information to all investigators. If relevant, all affected subjects shall be asked to confirm their continuing informed consent in writing.

9.2.6 Confidentiality

Confidentiality of subjects will be maintained throughout the study. A unique identification code will be assigned to each subject participating in this study. Any data that may be published in abstracts, scientific journals, or presented at

medical meetings will reference a unique subject code and will not reveal the subject's identity. The Sponsor, CRO, Investigators and Site personnel will make every reasonable effort to protect the confidentiality of all subjects participating in the study.

9.3 Insurance

The Sponsor will maintain the appropriate and necessary insurance coverage for the duration of the study.

9.4 Audits and Inspections

The Principal Investigator will also allow representatives of the governing EC, CA, U.S. Food and Drug Administration, and other applicable regulatory agencies to inspect all study records, CRFs, and corresponding portions of the subject's office and/or hospital medical records at regular intervals throughout the study. These inspections are for the purpose of verifying adherence to the CIP, completeness and exactness of the data being entered onto the CRFs and compliance with regulatory agency regulations.

The Principal Investigator will inform the Sponsor or the Sponsor's designee should they be audited or inspected by any regulatory agencies. The Sponsor or the Sponsor's designee will also inform the site if they are made aware of a pending audit or inspection by a regulatory agency.

9.5 Sponsor Responsibilities

Sponsor has the overall responsibility for the study and will:

- Select qualified Investigators, clinical investigators and study sites.
- Select qualified monitors.
- Provide the CIP and any subsequent amendments.
- Provide appropriate information and Investigational system training to the Investigator and study site staff.
- Ensure that all deviations from the CIP are reviewed with the appropriate Investigator(s) and reported on the CRFs and the final clinical report and that any necessary preventative or corrective action is taken.
- Ensure that all AEs and all ADEs are reported and reviewed with the Investigator(s), and where appropriate, that all SAEs and all SADEs are appropriately reported.
- Ensure that all Device Deficiencies / Malfunctions are reviewed by the Sponsor, and properly assessed and investigated, as appropriate.
- Promptly inform the Investigator and where applicable, any regulatory authorities, if the study is prematurely terminated or suspended and the reason for the termination or suspension.
- Ensure proper device usage, uniform data collection and protocol compliance.
- Provide site initiation training to include review of the FARAPULSE Ablation System Plus Instructions for Use, the Clinical Investigation Plan, CRF

instructions, CRFs, AE/SAE/Device Deficiency reporting and requirements for obtaining informed consent.
- Provide the FARAPULSE Ablation System Plus to the participating study site, in quantities to support study activities.
- Coordinate ongoing communication with CROs, consultants and study site to resolve any problems concerning the protocol or data collection
- Every effort will be made to ensure compliance with the protocol.
- Retain ownership of all clinical data generated in this study and control the use of the data for purposes of regulatory submissions to CAs.
- Protect subject confidentiality.
- Provide Regulatory Site Binder to site.

9.6 Monitor Responsibilities

Clinical monitors, qualified by training and experience, will be responsible for monitoring and overseeing the conduct of the study.

Site Initiation Visit: Sponsor personnel and / or clinical monitors will conduct site initiation visits at the investigational site to ensure that the Principal Investigator and other investigational site personnel involved in the conduct of this investigation have received and understood the requirements and contents of this Clinical Investigation Plan, the Investigator's Brochure, the patient ICF, the CRFs, CRF Instructions, AE/SAE/Device Deficiency reporting requirements, and the Instructions for Use and the Institution and/ or Investigator Agreement.

Site Monitoring: The clinical monitors will conduct routine on-site monitoring visits and phone calls in accordance with a Study Monitoring Plan to evaluate compliance with the CIP, any specific recommendations made by the site's EC and the signed Institution and/or Investigator Agreement and to ensure that the CIP is being followed and that any protocol deviations are properly documented on the respective CRF. Clinical monitoring will include a verification that informed consent was properly obtained and documented for all enrolled study participants, a review of clinical records and CRFs for accuracy and completeness, resolution of missing or inconsistent results and a review of source documents.

Clinical monitoring will include a review of all adverse events, SAEs and Device Deficiencies / Malfunctions to ensure that all information has been reported to the Sponsor, EC and regulatory authorities as required by the Clinical Investigational Plan and applicable standards and laws.

The clinical monitor will verify that the CRFs are complete and in agreement with the source documentation and other records. The clinical monitor will ensure that all CRFs have been signed and dated by the Investigator.

The Investigator will make available to the clinical monitor for review all ICFs, all CRFs, source documentation and other relevant records for all enrolled subjects at the site. It is important that the Investigator and other relevant site personnel are available for consultation with the clinical monitors during the monitoring visits and that sufficient time is devoted at the site for the monitoring process.

If a deficiency is noted during an on-site visit or at any other time during the course of the study, the clinical monitor is required to discuss the situation with the Investigator and the Sponsor, and to subsequently monitor the implementation of corrective actions that are required to address the situation.

All monitoring activities will be documented by the clinical monitor in a Monitoring Report and will include, at a minimum, the date, investigational site visited, names of all personnel involved in the visit, a listing of all documents reviewed and a summary of all findings, facts, deviations, conclusions and recommended actions to be taken. Key findings will be reviewed with the clinical investigator.

Upon completion of the study, a study closeout visit will be conducted to ensure that all data collection and study requirements are complete.

9.7 Investigator Responsibilities

At a minimum, the following documents will be provided by the investigational site to the Sponsor prior to study start (consent of the first subject):

- Signed Clinical Trial Agreements
- Signed Financial Disclosure Form
- Signed Clinical Investigation Plan Signature Page
- Investigator and Co-Investigator's current Curriculum Vitae
- Any other additional documents as required by the Sponsor

The Investigator is responsible for ensuring that the investigation is conducted according to all signed agreements, the CIP, governing regulations, data protection regulations, medical device laws, the Declaration of Helsinki and any other conditions imposed by the relevant regulatory authorities. The Investigator is responsible for maintaining medical and study records for every subject participating in the clinical study (including information maintained electronically such as digital imaging). The Investigator will also maintain original source documents from which study-related data are derived.

The Investigator(s) shall be responsible for the day to day conduct of the investigation as well as for the safety and well-being of the human subjects involved in the clinical investigation.

The Investigator(s) shall:

- Have the qualified and trained resources to conduct the investigation properly.
- Obtain from the Sponsor the information which the Investigator(s) judges essential about the device and be familiar with this information.
- Be well acquainted with the CIP before signing the signature page.
- Support the monitor, auditor, if applicable, in their activities to verify compliance with the CIP, to perform source data verification and to correct the CRF where inconsistencies or missing values are identified.
- Discuss with the Sponsor management any question of modification of the CIP.

- Make sure that the CIP is followed by all responsible for the conduct of the study at his/ her institution. Any deviation shall be documented and reported to the study Sponsor and CRO.
- Make the necessary arrangements to ensure the proper conduct and completion of the investigation.
- Make the necessary arrangements for emergency treatment, as needed, to protect the health and welfare of the subject.
- Ensure that appropriate EC and CA approval is obtained prior to the start of the investigation.
- Inform Sponsor about adverse events and Device Deficiencies / Malfunctions in a timely manner; document on applicable CRFs.
- Endeavor to ensure an adequate recruitment of subjects.
- Ensure that the subject has adequate information and time to provide informed consent.
- Ensure that informed consent is obtained and documented on the EC-approved ICF.
- Ensure that clinical records are clearly marked to indicate that the subject is enrolled in this study.
- Provide subjects with well-defined procedures for any emergency situation and safeguard the subject's interest. Under these circumstances, deviations from the CIP shall not require the prior approval of the Sponsor or the national and local regulatory authorities. Such deviations shall not be considered as a breach of agreement but shall be documented and reported to Sponsor.
- Ensure that information which becomes available as a result of the clinical investigation which may be of importance to the health of a subject and the continuation of the investigation shall be made known to the Sponsor and, if pertinent to the safety or well-being of the subject, and the private clinician.
- Inform the subject and/ or the subject's physician about any premature termination or suspension of the investigation with a rationale for study termination.
- Have primary responsibility for the accuracy, legibility and security of all investigation data, documents and subject records both during and after the investigation.
- Sign each subject's CRF, as applicable.
- Be responsible for the supervision and assignment of duties at his/ her clinical center.
- Ensure that all investigational devices are kept in a secure location and that all Systems are accounted for on the Device Accountability Form (number of devices used, discarded and returned to Sponsor).
- Investigator shall assign responsibility of Regulatory Site Binder and its maintenance to the Research Study Coordinator.

9.8 Investigator Training

The participating investigator will be trained in the use of the FARAPULSE Ablation System Plus prior to participating in the study. Device training will be

conducted by the Sponsor or its representatives. All device training will be documented in a training log that will be maintained in the Regulatory Site Binder.

9.9 Site Training

To ensure accurate, complete and reliable data, the Sponsor or its representatives will provide instructional material to the site, as appropriate; instruct the investigator and study personnel on the CIP, the completion of the CRFs including CRF Instructions, and study procedures; communicate regularly with site personnel via mail, email, telephone, and/or fax; and make periodic monitoring visits to the site. During those visits, the Sponsor or its representatives will monitor the subject data recorded in the CRFs against the source documents at the site for all enrolled subjects.

9.10 Clinical Events and Data Monitoring Committee

The Sponsor has established an external group of expert physicians who are not investigators to serve as the Clinical Events and Data Monitoring Committee (CEDMC). This group will consist of a panel of 3 experienced, independent physicians who are not investigators and who will be supported by the Medical Monitor and Study Statistician. A combined committee is an appropriate structure for a 50 subject feasibility study.

The CEDMC will convene during the study to screen, classify and adjudicate all adverse events reported in the subject investigation as well as major study outcomes. The CEDMC will be provided with case summaries, relevant source documents and any other information required to evaluate and adjudicate the adverse events and study outcomes.

The CEDMC will also convene to review safety data and trends during the conduct of the study. This formal assessment will occur at a minimum after the enrollment of 15 and then 50 subjects. The CEDMC will recommend to the Sponsor whether a study pause or termination is required if it identifies a trend that indicates a danger to patient safety.

9.11 Data Management

Data management procedures will be included in the Study Management Plan.

eCRFs will be made available to the participating site. Investigators are responsible for the accurate completion of patient eCRFs during the study. The Investigator will ensure that complete, accurate and timely data in eCRFs are completed, that protocol requirements are followed, and that complications, adverse events and adverse device effects are correctly reported and investigated, as appropriate. The Investigator is expected to maintain all source documents as required by the CIP, including laboratory results, supporting medical records, and signed ICFs. The source documents will be used during the regular monitoring visits to verify information against data contained in the completed eCRFs. eCRF data will be reviewed to identify any inconsistent or missing data and any adverse events. Any data issues are to be promptly addressed with the Investigator by the CRO.

After eCRF Monitoring has been complete and deficiencies / discrepancies resolved, study data in the central database will be updated to reflect any changes.

9.12 Study Suspension or Early Termination

The study can be discontinued at any site at the discretion of the Investigator or study Sponsor for reasons including, but not limited to, the following:

- Occurrence of adverse events unknown to date in respect to their nature, severity, or duration, or the unexpected incidence of known adverse events.
- Obtaining new scientific knowledge that shows that the study is no longer valid or necessary.
- Data demonstrates a benefit to subjects who undergo percutaneous ablation with the FARAPULSE Ablation System Plus making treatment without the FARAPULSE Ablation System Plus unethical.
- Insufficient recruitment of subjects.
- Unanticipated adverse device effect (UADE) presenting an unreasonable risk to subjects (Sponsor may terminate the study immediately)
- Persistent non-compliance with the Clinical Investigation Plan.
- Persistent non-compliance with regulatory requirements.

If the study is discontinued or suspended prematurely, the Sponsor shall promptly inform the clinical investigator/ investigational center of the termination or suspension and the reason(s) for discontinuation / suspension. The national and local regulatory authorities shall also be informed promptly and provided with the reason(s) for the termination or suspension by the Sponsor, CRO or by the clinical investigator/ investigation center. Further, if the study is discontinued or suspended prematurely, patients enrolled to that point will continue to be followed for safety through the 12-month timepoint.

9.13 Criteria for Suspending/ Terminating a Study Center

Sponsor reserves the right to stop the screening of subjects at the study center at any time after the study initiation visit if no subjects have been enrolled or if the center has multiple or severe protocol violations without justification or fails to follow remedial actions.

Possible reasons for suspending/ terminating the study center include, but are not limited to:

- Repeated failure to complete CRFs prior to scheduled monitoring visits;
- Failure to obtain written informed consent using the EC-approved ICF;
- Failure to report SAEs/ USADEs to Sponsor within 24 hours of knowledge;
- Loss of (or unaccounted for) investigational product inventory or repeated failure of device accountability.

9.14 Deviations from the Clinical Investigation Plan

Under emergency circumstances, deviations from the CIP to protect the rights, safety, and well-being of human subjects may proceed without prior approval of the Sponsor or EC.

The Investigator must notify the Sponsor and the CRO of any deviation from the CIP and document the reason for the deviation in the eCRF.

The Investigator shall notify the Sponsor and the reviewing EC of any deviation from the CIP, as per national requirements, to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than five (5) working days after the emergency occurred.

10. Regulatory Considerations

10.1 Maintaining Records

The Sponsor and CRO will maintain copies of critical correspondence, regulatory approvals, Trial Master Files, clinical data, shipment of devices, adverse events, serious adverse events, serious adverse device effects and other records related to the clinical study.

Trial records will be maintained for a minimum of 15 years following the completion of research activities and closure of the study with Ethics Committees, whichever is longer.

10.2 Data Handling and Record Keeping

10.2.1 Source Documents

The Investigator must maintain detailed source documents on all subjects who are enrolled or who undergo screening in the study. Source documents include but are not limited to, subject medical records, hospital charts, clinic charts, investigator subject study files, as well as the results of diagnostic tests (e.g., laboratory tests, hemodynamic studies).

The following minimum information should be entered into the subject's medical record:

- The date the subject entered the study and the subject number.
- The Clinical Investigation Plan number and the name of the Sponsor.
- The date that Informed Consent was obtained and signed by the patient and Investigator.
- Evidence that the subject meets the study eligibility requirements (e.g., medical history, study procedures and/or evaluations).
- The dates of all study related subject visits.
- Evidence that required procedures and/or evaluations were completed.
- Use of any concurrent medications.
- Documentation of specific device used.
- Occurrence and status of any adverse events (AEs / SAEs)
- The date the subject exited the study and a notation as to whether the subject completed the study or was discontinued, including the reason for discontinuation.

10.2.2 Data Collection

The Investigator must maintain detailed records on all subjects who sign the ICF and begin the pre-procedure evaluation. Data for enrolled subjects is transcribed onto eCRFs provided by the Sponsor or designee. All data should be transcribed completely and promptly.

Study exit eCRF will be completed for all enrolled subjects, regardless of whether they did or did not complete the study (e.g., subject discontinuation, study termination). The Sponsor and investigational site will maintain all records

pertaining to this study in accordance with local and national regulations. Prior to the destruction of study records the Investigator or his representative shall contact the Sponsor to ensure that they no longer need to be retained. In addition, Sponsor shall be contacted if the Investigator plans to leave the investigational site so that arrangements can be made for the handling or transfer of study records.

10.3 Ethics Committee and Competent Authority Approval

Regulatory approvals must be obtained prior to enrollment of the first patient. The Sponsor is responsible for obtaining regulatory and local approvals for the study. The Sponsor or its designated representative will require a copy of any IC and CA correspondence, as well as the final approval letter from the EC and CA, where applicable.

An Investigator may not make CIP changes without prior approval by the Sponsor. All significant CIP changes that may affect the following must be submitted and approved by the EC and CA before initiating the change:

- Validity of the data or information resulting from the completion of the approved CIP
- Relationship of the likely subject risk to benefit relied upon to approve the CIP
- Scientific soundness of the CIP
- Rights, safety, or welfare of the human subjects involved in the investigation

The Sponsor will notify the investigational site of such changes to ensure the study continues to be conducted consistent with the approved CIP.

10.4 Procedure for Amending the CIP

The process of amending the CIP and/or related documents is the responsibility of the sponsor. The procedure for amending the CIP shall be as follows:

- The Sponsor, Investigator, or other relevant party (e.g. EC, CA, CEDMC) may recommend modification of the CIP.
- The Sponsor will then modify as necessary the CIP and any associated documents requiring amendment as a result of the modification(s).
- The Sponsor or designated CRO will then submit the revised CIP and any other affected documents to the EC and CA for approval, per regulation.
- Once all required approvals are obtained, the site will be trained to the latest approved version of the CIP and any other affected documents.

10.5 Device Accountability

The Investigator is responsible for maintaining a Device Accountability Log that will track device receipt, device usage for all subjects and device returns to Sponsor or designees. Information tracked will include date of device usage, subject ID, and lot number.

11. Publication Policy

The existence of this clinical study is confidential, and it should not be discussed with persons outside of the study. Additionally, the information in this document and regarding this study contains trade secrets and commercially sensitive information that is confidential and may not be disclosed unless such disclosure is required by regional or national law or regulations. Subject to the foregoing, this information may be disclosed only to those persons involved in the study who have a need to know, but all such persons must be instructed not to further disseminate this information to others. These restrictions of disclosure will apply equally to all future information supplied to you that is indicated as confidential.

The data generated by this clinical study are the property of the Sponsor and should not be disclosed without the prior written permission of FARAPULSE, Inc. These data may be used by FARAPULSE, Inc. now and in the future for presentation or publication at FARAPULSE, Inc.'s discretion or for submission to governmental regulatory agencies. FARAPULSE, Inc. reserves the right of prior review of any publication or presentation of data from the subject investigation.

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