PEFCAT: A Safety and Feasibility Study of the FARAPULSE™ Endocardial Ablation System to Treat Paroxysmal Atrial Fibrillation

CLINICAL INVESTIGATION PLAN (CIP) NUMBER: CS0267 REVISION D

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ISSUE DATE: 26 FEBRUARY 2019

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2. Executive Summary

SPONSOR NAME:	FARAPULSE, Inc.
TITLE OF STUDY:	PEFCAT: A Safety and Feasibility Study of the FARAPULSE Endocardial Ablation System to Treat Paroxysmal Atrial Fibrillation
PROTOCOL NUMBER:	CS0267
OBJECTIVE:	The objective of the safety and feasibility study is to demonstrate that the endocardial creation of electrically isolating lesions via pulsed electric field (PEF) catheter ablation applied using the FARAPULSE Endocardial Ablation System is a feasible and safe treatment for paroxysmal atrial fibrillation (PAF).
CLINICAL HYPOTHESIS:	Endocardial creation of electrically isolating lesions in cardiac tissue via PEF catheter ablation using the FARAPULSE Endocardial Ablation System is a feasible and safe treatment for paroxysmal atrial fibrillation (AF).
NAME OF INVESTIGATIONAL DEVICE:	FARAPULSE Endocardial Ablation System • FARAWAVE™ Endocardial Ablation Catheter System • FARASTAR™ Endocardial Generator System • FARADRIVE™ Deflectable Sheath System
DESIGN:	Prospective, multi-center, safety and feasibility study. Subjects will undergo percutaneous PEF ablation for pulmonary vein isolation. Subjects will then be followed at 7 days, 30 days, 75 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 80 subjects
CLINICAL SITES:	Nemocnice Na Homolce, Prague, Czech Republic Hopital cardiologique du Haut-Leveque, Pessac, France

DURATION OF PARTICIPATION:	Subjects will be followed at 7 days, 30 days, 75 days, 90 days, 6 months and 12 months with a 90-day blanking period for recurrent atrial fibrillation or atrial tachycardia following the initial PEF catheter ablation procedure. The enrollment period is estimated to take 9 months and subjects will be followed for up to 12 months. The total study duration will be approximately 21 months.
PLANNED PROCEDURE:	Subjects will undergo an attempt to isolate all 4 pulmonary veins or their anatomic equivalent. Subject with a past history of or having inducible isthmus-mediated flutter will undergo interruption of the cavo-tricuspid isthmus at the discretion of the investigator. Additional lesions may be made at the discretion of the investigator.
PRIMARY SAFETY ENDPOINT:	The primary safety endpoint for this study is the Composite Safety Endpoint (CSE) defined as the incidence of the following early-onset and late-onset serious adverse events (SAEs) which are device- or procedure-related: Early onset (within 30 days of any endocardial ablation for atrial fibrillation) • Death • Myocardial infarction (MI) • Persistent diaphragmatic paralysis • Stroke or transient ischemic attack (TIA) • Peripheral or organ thromboembolism • Pericarditis • Cardiac tamponade / perforation • Vascular access complications • Hospitalization (initial or prolonged)* • Heart block Late onset (any time during follow-up) • Pulmonary vein (PV) stenosis (> 70% diameter reduction from baseline) • Atrio-esophageal fistula * Excludes hospitalization (initial & prolonged) solely due to arrhythmia (AF/Atrial Flutter/Atrial Tachycardia) recurrence or due to non-urgent cardioversion (pharmacological or electrical). Hospitalization excludes visits to hospital-associated outpatient facilities such as clinics or emergency wards.

SECONDARY SAFETY ENDPOINT:	1. The proportion of subjects reporting one or more device- or procedure-related SAEs, as assessed at 30 days, 75 days, 6 months and 12 months of follow-up. 2. The proportion of subjects with stroke or TIA through 12 months 3. The proportion of subjects with major bleeding related to anticoagulation treatment through 12 months 4. The proportion of subjects requiring cardioversion through 12 months 5. The proportion of subjects requiring an arrhythmia-related hospitalization through 12 months
PRIMARY FEASIBILITY ENDPOINT:	The proportion of subjects that achieve Acute Procedural Success (APS) defined as the percutaneous endocardial creation of a complete, electrically isolating set of lesions around the ostia of the pulmonary veins (PVI) using the FARAPULSE Endocardial Ablation System during the first procedure, as clinically assessed by entrance and/or exit block performed ≥ 20 minutes after the last PVI lesion is made.
SECONDARY FEASIBILITY ENDPOINT:	1. The proportion of subjects that achieve Chronic Procedural Success (CPS) defined as persistent electrical isolation of all initially ablated pulmonary veins assessed during an electroanatomical mapping procedure performed 75 days following the index procedure. Chronic Procedural Success will be subdivided by single procedure and reablated subjects. 2. The proportion of subjects that achieve Therapeutic Success, defined as freedom from: a. Post blanking period through assessment: occurrence of AF, AFL or AT, or ablation for AF/AFL/AT using the study device b. At any time: ablation for AF/AFL/AT with a nonstudy device Therapeutic Success will be assessed from the end of the blanking period at Months 6 and 12 and will be subdivided by on / off AFDs (Atrial Fibrillation Drugs) post blanking period.

ADDITIONAL ENDPOINTS:

Additional endpoints will include:

1. Proportion of all ablated pulmonary veins that are isolated at the index procedure using the study device.
2. Proportion of all ablated pulmonary veins acutely isolated using the study device that remain isolated at the 75-day remapping procedure.

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 who have:
   a. Confirmed AF: Documentation may include ECG, transtelephonic monitor (TTM), Holter monitor, implanted devices, telemetry strip or similar, 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 AFD, meaning therapeutic failure of at least one antiarrhythmic drug (AFD; 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. Use of amiodarone within 3 months prior to enrollment
2. Atrial fibrillation that is any of the following
    a. Persistent (by diagnosis or duration > 7 days)
    b. Secondary to electrolyte imbalance, thyroid disease, alcohol abuse or other reversible / non-cardiac causes
    c. Requires ≥ 3 cardioversions in the preceding 12 months
3. Cardiac anatomical exclusions by imaging within 3 months prior to enrollment:
    a. Left atrial anteroposterior diameter ≥ 5.0 cm as documented by transthoracic echocardiography (TTE) or computed tomography (CT)
    b. Left ventricular ejection fraction ≤ 40% as documented by TTE
4. Any of the following cardiac procedures, implants or conditions:
    a. Clinically significant arrhythmias other than AF
    b. Hemodynamically significant valvular disease
    c. Prosthetic heart valve
    d. NYHA Class III or IV CHF
    e. Previous endocardial or epicardial ablation or surgery for AF
    f. Atrial or ventricular septal defect closure
    g. Atrial myxoma
    h. Left atrial appendage device or occlusion
    i. Pacemaker, ICD or CRT
    j. Significant or symptomatic hypotension
    k. Bradycardia or chronotropic incompetence
    l. History of pericarditis
    m. History of rheumatic fever
5. Any of the following within 3 months of enrollment:
    a. Myocardial infarction
    b. Unstable angina
    c. Percutaneous coronary intervention
    d. Heart surgery (e.g. coronary artery bypass grafting, ventriculotomy, atriotomy)
    e. Heart failure hospitalization
    f. Stroke or TIA
    g. Clinically significant bleeding
    h. Pericarditis or pericardial effusion
    i. Left atrial thrombus
6. History of blood clotting or bleeding abnormalities.

7. Contraindication to, or unwillingness to use, systemic anticoagulation
8. Contraindications to CT or MRI
9. Sensitivity to contrast media not controlled by premedication
10. Women of childbearing potential who are pregnant, lactating or not using birth control
11. Serious or untreated medical conditions that would prevent participation in the study, interfere with assessment or therapy, or confound data or its interpretation, including but not limited to
    a. Solid organ or hematologic transplant, or currently being evaluated for an organ transplant
    b. Severe lung disease, pulmonary hypertension, or any lung disease involving abnormal blood gases or significant dyspnea
    c. Chronic renal insufficiency of < 60 mL/min/1.73 m^2, any history of renal dialysis, or history of renal transplant
    d. Active malignancy or history of treated cancer within 24 months of enrollment
    e. Clinically significant gastrointestinal problems involving the esophagus, stomach and/or untreated acid reflux
    f. Clinically significant infection
    g. Predicted life expectancy less than one year
12. Clinically significant psychological condition that in the investigator's opinion would prohibit the subject's ability to meet the protocol requirements
13. Current or anticipated enrollment in any other clinical study
14. Body Mass Index (BMI) > 35
15. Distorted cardiac anatomy due to congenital heart disease

Abbreviations

ACT Activated clotting time
AE Adverse Event
AF Atrial fibrillation
AFD Atrial Fibrillation Drug
AFL Atrial flutter
APS Acute procedural success
AT Atrial tachycardia
CHF Congestive heart failure
CPS Chronic procedural success
CT Computed tomography
DCCV Direct current cardioversion
ECG Electrocardiogram
INR International normalized ratio
LA Left atrium
MI Myocardial infarction
MRI Magnetic resonance imaging
NYHA New York Heart Association
PAF Paroxysmal atrial fibrillation
PEF Pulsed electric field
PTT Prothrombin time
PV Pulmonary vein
PVI Pulmonary vein isolation
PVS Pulmonary vein stenosis
TEE Transesophageal echocardiography
TIA Transient ischemic attack
TTE Transthoracic echocardiography
TTM Transtelephonic monitor

3. Introduction

3.1 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 mortality rate for patients with atrial fibrillation is twice that of patients in whom normal sinus rhythm is maintained. 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). Last, AF remains an extremely costly public health burden, with annual per patient cost of care approaching €3000 (approximately U.S. $3200).[7] Atrial fibrillation is characterized by abnormalities in electrical impulse formation or conduction within the heart; these abnormalities disrupt the heart's coordinated mechanical contraction and can result in reduced or insufficient cardiac output or other complications.[8] Symptoms arising from this arrhythmia include palpitations, shortness of breath, fatigue, syncope, or intolerance to exertion.

According to the Heart Rhythm Society (HRS) 2012 Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation, AF is clinically stratified by whether episodes are self-terminating (paroxysmal) or continuous (persistent or permanent AF).[9] Paroxysmal AF (PAF) is defined as recurrent AF (≥2 episodes) that terminates spontaneously within 7 days, or within 48 hours if terminated by pharmacologic or electrical cardioversion. Persistent AF is defined as continuous AF that is sustained beyond 7 days, or less than 7 days but terminated by pharmacologic or electrical cardioversion. Longstanding persistent AF is defined as continuous AF of greater than 12 months' duration. Permanent AF is defined as AF in a patient in whom a decision has been made not to restore or maintain sinus rhythm by any means.

Initial treatment of PAF is typically directed toward heart rate or rhythm control with drug therapy and direct current cardioversion (DCCV). As a reasonable alternative to restoring sinus rhythm via long-term pharmacologic therapy, catheter ablation is being performed with greater frequency. Three recent small randomized trials in patients with PAF demonstrated that catheter ablation was superior to antiarrhythmic therapy in the prevention of recurrent AF.[10, 11, 12] This was followed by the more recent Navistar ThermoCool® Catheter and EZ Steer ThermoCool® NAV Catheter PMA submission substantiating the findings in a larger series.[13]

Although it is still the consensus recommendation that catheter ablation should not be considered a first line therapy for atrial fibrillation,[13] there is evidence that maintenance of sinus rhythm has important effects on mortality. In the Atrial

Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial, in which 4,060 AF patients with high risk for stroke and death were randomized to either rhythm control or rate control by antiarrhythmic drugs, there were no significant differences in all-cause death between the two strategies.[14] However, a new on-treatment analysis of the AFFIRM study revealed that the presence of sinus rhythm was associated with a significant reduction in mortality, whereas the use of antiarrhythmic drugs increased mortality by 49%,[15] suggesting that the beneficial effect of sinus rhythm restoration on survival might be offset by the adverse effects of antiarrhythmic drugs.

Ablation treatment paradigms have evolved over time, and current strategies emphasize isolation of the pulmonary veins (PVI) as the cornerstone of catheter ablation of AF. Energy sources for endocardial lesion creation have included radiofrequency, cryo (freezing), laser, ultrasound and microwave. New ablation techniques and devices continue to develop with the objective of improving safety and efficacy, while reducing procedure time (complexity). In elite single-center reports, the success rate for eliminating symptomatic AF (inclusive of both PAF and continuous AF subjects) varies from 55% - 77%, with many patients requiring multiple procedures.[16, 17, 18, 19] Retreatment rates as high as 40% have been reported.[20]

Understanding the need for creating electrical isolation of the pulmonary veins, treatment paradigms have focused on creating circumferential lesions or wide circumferential lesion sets that block electrical continuity between the pulmonary veins and the left atrium. In a wide circumferential ablation (WACA) procedure, operators must form a contiguous line of electrical block around ipsilateral pulmonary veins using fluoroscopic guidance and electroanatomical mapping technologies. A limited assessment of lesion formation and position is determined by monitoring voltage reduction of the local electrogram at the target site. Electrical gaps in lesion sets occur frequently, leading to recurrent AF and/or creation of substrate susceptible to reentrant atrial tachycardias.[21] Ablation technologies that rely upon indirect assessment of lesion formation are challenged to deliver improved durability and therefore long-term efficacy of therapy.

3.2 Surgical and Catheter Ablation

Cox and colleagues are credited with developing and demonstrating the efficacy of surgical ablation of AF via the "maze" or "Cox-maze" procedure (sometimes also referred to as the “traditional maze” or “cut-and-sew maze”), an open-heart cardiac surgery procedure intended to eliminate AF, by a series of incisional scars in both atria, to block abnormal electrical circuits (atrial macroreentry), a requisite AF mechanism. During the Cox-Maze Procedure, areas of cardiac tissue are isolated, either by cut and sew methods or electrosurgically, creating a “maze” which prevents propagation of ectopic AF impulses[22, 23] notes: “While few patients are candidates for a stand-alone surgical procedure to cure AF using the maze or LA ablation techniques, these approaches can be an effective adjunct to coronary bypass or valve repair surgery to prevent recurrent postoperative AF.”

Reported failure rates for the maze procedure are as high as 30%. Jais 2002 summarized the conclusions from surgical treatments for AF.[24]

- reduction of the atrial tissue mass available for fibrillation is effective in preventing maintenance of AF;
- the left atrium plays a dominant role in maintenance and initiation of AF;
- limited lesions placed around pulmonary veins can be as effective as complex ablation schema (maze)and safer.

However, Wisser 2007 reported results of a small non-randomized study comparing two groups of patients, all treated surgically for permanent AF at the same time as other major heart surgery. Group 1 (N=29) received a classic maze procedure: freedom from AF at 19 months follow up was 86%. Group 2 (N=43) received epicardial pulmonary vein isolation treatment, and freedom from AF at follow up was 59%. This difference was statistically significant.

Due to the extreme complexity of the "cut and sew" Cox-Maze procedure, few surgeons perform the surgery. Instead, minimally invasive surgical techniques have been developed. The FAST trial randomized antiarrhythmic drug-refractory AF patients to minimally invasive surgical ablation or catheter ablation.[25] Outcomes for efficacy and safety during a 12-month follow-up demonstrated an overall increased freedom from AF in the minimally invasive surgery group compared to the catheter ablation cohort; however, the surgical ablation group had significantly more procedural-related adverse events compared to catheter ablation (23.0% versus 3.2%).

During the past decade, the evolution of catheter-based energy delivery (such as radiofrequency and cryothermia) has evolved as a non-surgical means to create similar lesions in the walls of the atria (i.e., Cox maze IV ablation-assisted procedure).[26] However, electrophysiologists have found it challenging to replicate the Cox Maze III in its entirety.

Pulmonary vein isolation (PVI), which is the cornerstone of the mini-maze procedure and catheter ablations, essentially creates "boxes" around the four pulmonary veins. PVI catheter ablation as a treatment for paroxysmal AF is associated with a high rate of success, in excess of 70%; however, outcomes for treating persistent AF with PVI are substantially lower and often require multiple procedures to maintain long-term freedom from atrial arrhythmias. While electrical isolation of the pulmonary veins (PVs) is central to catheter ablation strategies, foci and/or substrate outside the PVs, particularly in the LAA, have been identified as a key mechanism in the maintenance of persistent AF.[27, 28, 29, 30]

The literature suggests that catheter ablation is more efficacious for those patients with paroxysmal AF in comparison to those with persistent forms of AF.[31] This may in part be due to the finding that in many of these patients, and with new mapping technologies, specific foci may be identified and treated.[32, 33]

3.3 Irreversible Electroporation (IRE)

Al-Sakere 2007[34] 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.[35 36 37 38] IRE ablation typically spares the extracellular matrix, which facilitates rapid wound healing.[39, 40, 41, 42, 43]

Thomson 2011[44] reported a case-series study (N=38) assessing the safety of irreversible electroporation (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[45] (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[46] (N=6) confirmed this result out to 3-month follow up. Neven 2014[47] (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.

3.4 Summary of FARAPULSE Clinical Studies

3.4.1 FARAPULSE Endocardial Ablation Clinical Studies

FARAPULSE IMPULSE Clinical Study
FARAPULSE, Inc, has 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; the same system which will be used in the subject investigation. Thirty-eight (38) patients have been enrolled between January and November of 2018. All patients were discharged in good condition. One patient was treated for tamponade at the conclusion of the index procedure. The event was resolved. One patient was treated for a supraventricular tachycardia seven months post procedure. The event was resolved. One patient underwent extended hospitalization for an early AF recurrence one day

post procedure. The event was resolved. At the conclusion of the index procedure all (100%) pulmonary veins (PVs) were isolated using the FARAPULSE device. Twenty-four (24) patients have returned for the protocol-defined 3-month remapping procedure to assess chronic PV isolation. Among these patients, 61% of PVs remained isolated at the 3-month remapping procedure. All PVs in eight (8) patients remained isolated. These results support both the safety and performance of the system.

FARAPULSE PEFCAT Clinical Study (same as subject investigation)
FARAPULSE, Inc, has also initiated a safety and feasibility study at Na Homolce Hospital in Prague, Czech Republic under the "PEFCAT" Protocol, CS0267. This safety and feasibility study is the same investigation that is being proposed for Pessac, France. This study is being conducted using the FARAPULSE Endocardial Ablation System; the same system which will be used in the subject investigation. Sixteen (16) patients have been enrolled at Na Homolce between October and November of 2018. All patients were discharged in good condition. One patient was treated for an air embolism during the index procedure. This event was resolved.. At the conclusion of the index procedure all pulmonary veins (PVs) were isolated using the FARAPULSE device.

3.4.2 FARAPULSE Epicardial Ablation Clinical Studies

FARAPULSE FIM Epicardial Clinical Study
In addition, FARAPULSE has shown the preliminary safety and feasibility of Pulsed Electrical Field ablation in an earlier clinical study using the FARAPULSE Cardiac Ablation System for epicardial ablation between September 2016 and March 2017. The data collected in this first study using the epicardial system has supported and informed the design of the FARAPULSE Endocardial Ablation System. Below is a summary of FARAPULSE's First-in-Man (FIM) clinical study entitled, "First in Human- Phase 1 / 1A safety study of the FARAPULSE, Inc. Cardiac Ablation System used for cardiac tissue ablation for the treatment of atrial fibrillation through open heart surgical procedure."

This first study was initiated at the Italian Hospital, Asuncion Paraguay in September 2016. Seven (7) patients were enrolled in the study, each patient had been diagnosed with paroxysmal, persistent and/or continuous atrial fibrillation and was scheduled for a cardiac surgery procedure. The purpose of this FIM study was to investigate the safety and acute technical feasibility of the FARAPULSE Cardiac Ablation System to perform epicardial cardiac ablation in treating patients with atrial fibrillation (AF).

Following Ethics Committee approval, patient consent and enrollment in the study, clinical evaluations were conducted and data collected at the following intervals: pre-procedure (baseline), post-procedure, hospital discharge, and 30 day, 3-months (optional), and 6-months post-procedure. The FARAPULSE procedural clinical data were collected and recorded on standardized case report forms at the clinical study site.

There were no device or ablation procedure-related adverse events reported within 7-days post-procedure or at time of discharge. Also, there were no device malfunctions. Additionally, electrical isolation of the pulmonary veins and the posterior left atrium using the FARAPULSE Cardiac Ablation System was achieved in three of seven (3/7) patients. These findings demonstrate the safety and feasibility of applying pulse electrical field energy to the heart to ablate electrically

active myocardium and isolate the pulmonary veins. The same application of energy has been used for endocardial ablation in atrial fibrillation in the IMPULSE study.

FARAPULSE IMPACT Clinical Study
In addition, FARAPULSE, Inc. is conducting a safety and feasibility study of the FARAPULSE Cardiac Ablation System at Na Homolce Hospital in Prague, Czech Republic and CHU Bordeaux in Pessac, France under the "IMPACT" Protocol, CS0172. Seven (7) patients have been enrolled between December 2017 and March 2018, four (4) in Prague and three (3) in Bordeaux. All patients were discharged in good condition. One femoral hematoma was noted, which was not investigational device related. The event was resolved. One hospitalization for atrial tachycardia was noted eight months post procedure. The event was resolved.

At the conclusion of the index procedure the posterior left atrium and PVs were isolated in six (6) of seven (7) patients. Six (6) patients have reached the 3-month follow-up assessment. The posterior left atrium and PVs were electrically isolated in one of these patients. In two of the remaining patients there was a small electrical gap, which was closed at the 3-month follow-up using a commercial radiofrequency catheter. In one of these patients, the gap had been present at the conclusion of the index procedure; in the other patient the gap had developed during the follow-up period. Three (3) patients undergoing remapping required multiple radiofrequency lesions at the three-month follow-up. Patients in this protocol will undergo follow-up at 30 days, 3 months, 6 months, and 12 months.

3.5 Complications of Catheter Based and Surgical Ablation

The risks and complications associated with thermal or non-thermal cardiac ablation depend on the complexity of the procedure. The most common complications due to cardiac ablations include bleeding, cardiac tamponade, stroke/TIA, pulmonary vein stenosis, phrenic nerve injury, thromboembolism, air embolism, post-procedural arrhythmias, and vascular complications. Further, recurrences of atrial fibrillation (AF) or atrial tachycardia after an initial AF catheter ablation procedure (20 – 40% of patients[48]) are common.

Gelsomino 2014[49] noted in a study of SAEs (Serious Adverse Event) rates for studies of convergent AF ablation (N=335) (**Table 1**). There were 3 early deaths (0.9%) and three conversions to sternotomy and cardiopulmonary bypass (0.9%). There were no late deaths or thromboembolic events. These SAE rates include both catheter ablation and surgical ablation procedures in the reviewed studies. Expected adverse event rates from an isolated surgical procedure are likely to be lower.

Table 1: Data from Gelsomino 2014 – Adverse Event Rates for Surgical Ablation

Event	Frequency (%)
Bleeding	6 (1.8%)
Tamponade	4 (1.2%)
Pleural effusion	1 (0.3%)
Hemothorax	1 (0.3%)
Pneumothorax	1 (0.3%)
Pneumonia	1 (0.3%)

In conclusion, potential risks related to the FARAPULSE Endocardial Ablation System are expected to be no different from those products that are approved and available on the market for catheter-based or surgical ablation procedures. FARAPULSE testing of the Endocardial Ablation System will ensure the safe use of the device during clinical investigation as well as compliance with the applicable parts of the Medical Device Directive 93/42/EEC. FARAPULSE will also ensure, through its Risk Management System, that the residual risks have been reduced as low as possible. The prior clinical experience using the FARAPULSE Endocardial Ablation System as well as a review of the complications associated with catheter-based cardiac ablation procedures support the execution of this study to further assess the safety and feasibility of the FARAPULSE Endocardial Ablation System.

4. Investigational Device

4.1 Name of Investigational Device

FARAPULSE Endocardial Ablation System

4.2 Intended Use

The FARAPULSE Endocardial Ablation System is indicated for cardiac tissue ablation for the treatment of paroxysmal atrial fibrillation.

4.3 Classification

The FARAPULSE Endocardial Ablation System is comprised of the FARAWAVE Endocardial Ablation Catheter System, the FARASTAR Endocardial Generator System, and the FARADRIVE Deflectable Sheath System.

The FARAWAVE Endocardial Ablation Catheter System is classified as a Class III medical device. Per MDD 93/42/EEC Annex IX Rule 6 applies to the ablation catheter, which defines it as a surgically invasive device 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 Endocardial Generator System is classified as a Class IIb medical device. Per MDD 93/42/EEC Annex IX Rule 9 applies to the generator system,

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 Deflectable Sheath System is classified as a Class III medical device. Per MDD 93/42/EEC Annex IX Rule 6 applies to the Deflectable Sheath System, which defines it as a surgically invasive device 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.

4.4 System Components: FARAPULSE Endocardial Ablation System

The FARAPULSE Endocardial Ablation System used in the subject clinical investigation consists of the FARAWAVE Endocardial Ablation Catheter System, the FARASTAR Endocardial Generator System, and the FARADRIVE Deflectable Sheath System (**Figure 1**). Model (REF#) numbers of the components used in this study are detailed in **Table 2**.

Table 2: Components and Model Numbers of the FARAPULSE Endocardial Ablation System

System Components	System Model Number (REF#)
FARAWAVE Endocardial Ablation Catheter System 1. Ablation Catheter (31 mm or 35 mm) 2. Extension Cable	40T401 and 40T404
FARASTAR Endocardial Generator System 1. Pulsed Electric Field Generator (PEFG) 2. Two Coaxial Cables 3. Two Pace Filter Boxes 4. Two Catheter Switch Boxes	60T401
FARADRIVE Deflectable Sheath System (or commercially available CE Marked Deflectable Sheath System such as the CE Marked Oscor Destino™ Twist UniDirectional Deflectable Guiding Sheath)* 1. Sheath 2. Dilator	20T401

CE Marked Devices That May be Used in Conjunction with FARAPULSE Endocardial Ablation System
*Oscor Destino™ Twist UniDirectional Deflectable Guiding Sheath
St. Jude BRK 98cm Transseptal Needle
MicroPace StimCor Cardiac Stimulator

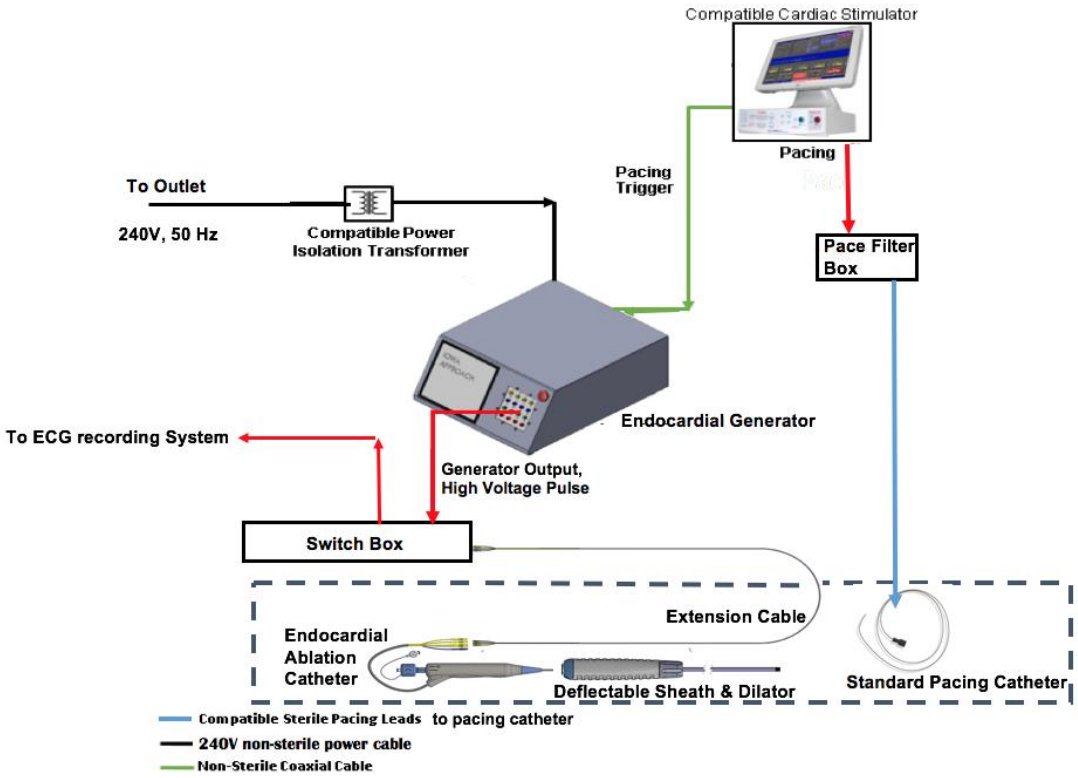

Figure 1. FARAPULSE Endocardial Ablation System Components.
Note: Blue dotted box shows the sterile, single-use components of the system

4.4.1 FARAWAVE Endocardial Ablation Catheter System

The FARAWAVE Endocardial Ablation Catheter System 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 40T401) and 35mm (REF 40T404) 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 System. It consists of a multi-electrode ablation catheter with electrodes arranged on splines. The Ablation Catheter consists of a distal section with five splines that deploy into a flower-shaped configuration with five petals, a shaft section, and a proximal handle with a manually operated deployment control (**Figure 2**). Each petal has a single electrode that is separately wired to facilitate connection to a mapping or recording system (this is an optional feature offered to the user). 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 cable with connectors. The catheter connectors connect to an Extension cable (also part of the Endocardial Ablation

Catheter System) with numbered connectors on each of its ends. These connect to the multi-channel Endocardial Generator. The Pulsed Electric Field energy is delivered via the PEF Generator over the set of ablation catheter electrodes. The Extension Cable is a single-use sterile cable that provides additional cable length to connect to the Endocardial Generator.

Additional details are provided in the IFU LBL0195 for the specific use and procedural steps of the Endocardial Ablation Catheter System.

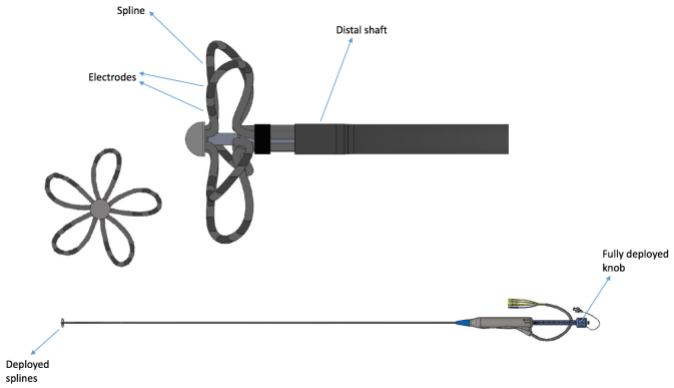

Figure 2: Representative Illustration of Deployed Endocardial Ablation Catheter with Fully Deployed Distal "flower" Section. Provided in 31mm and 35mm Deployed Diameters

4.4.2 FARASTAR Endocardial Generator System

The FARASTAR Endocardial Generator System consists of the following components – Pulsed Electric Field Generator (PEFG), BNC Coaxial Cable (2 units), Pace Filter Box (2 units), and Switch Box (2 units). The Endocardial Generator System is designed to deliver Pulsed Electric Field (PEF) energy to endocardial sites in the heart via the Endocardial Ablation Catheter System and other compatible devices (refer to IFU LBL0195 for the specific use and procedural steps of the Endocardial Ablation Catheter System, LBL0193 for the Deflectable Sheath System and LBL0198 for the Endocardial Generator System).

The Pulsed Electric Field Generator is a 16-channel output unit that generates a pulsed voltage waveform that can be delivered to the ablation catheter electrodes. The FARASTAR Generator, while capable of operating between 1400V and 2100V, currently allows ablation energy in discrete user-selectable voltage settings between 1400V and 2000V.

As an input, a compatible cardiac stimulator unit for cardiac pacing is applied to the cardiac chambers via pacing catheters and to the PEFG with a coaxial cable to synchronize the application of therapeutic PEF energy to the actively paced heart. The physician confirms proper synchronization by actuating a button on the

PEFG user interface. The BNC Coaxial Cable is used to connect the generator to a commercially available compatible cardiac stimulator/pacing device.

Details regarding the generator are provided in the FARASTAR Endocardial Generator System User Manual LBL0198.

4.4.3 FARADRIVE Deflectable Sheath System

The FARAWAVE Endocardial Ablation Catheter is used with the FARADRIVE Deflectable Sheath System or a compatible CE Marked Deflectable Sheath System (13F) such as the CE Marked Oscor Destino™ Twist UniDirectional Deflectable Guiding Sheath.

The FARADRIVE Deflectable Sheath System consists of two (2) components: Deflectable Sheath and Dilator, which are used together. Both components are sterile and single use only (**Figure 3**).

The 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 3: Deflectable Sheath and Dilator

4.5 Device Accountability

The FARAPULSE Endocardial Ablation System will be housed 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 Endocardial Ablation System

identification number (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.

4.6 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.

5. Study Objectives

The objective of the safety and feasibility study is to demonstrate that the endocardial creation of electrically isolating lesions via pulsed electric field (PEF) catheter ablation applied using the FARAPULSE Endocardial Ablation System is a feasible and safe treatment for paroxysmal atrial fibrillation (PAF).

5.1 Study Design

This is a prospective, multi-center, intention-to-treat safety and feasibility study. Subjects will undergo percutaneous PEF ablation for pulmonary vein isolation. Subjects will then be followed at 7 days, 30 days, 75 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.

5.2 Selection and Withdrawal of Subjects

5.2.1 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; who have:

   a. Confirmed AF: Documentation may include ECG, transtelephonic monitor (TTM), Holter monitor, implanted devices, telemetry strip or similar, 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 AFD, meaning therapeutic failure of at least one antiarrhythmic drug (AFD; 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.

5.2.2 Exclusion Criteria

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

1. Use of amiodarone within 3 months prior to enrollment
2. Atrial fibrillation that is any of the following
   a. Persistent (by diagnosis or duration > 7 days)
   b. Secondary to electrolyte imbalance, thyroid disease, alcohol abuse or other reversible / non-cardiac causes
   c. Requires ≥ 3 cardioversions in the preceding 12 months
3. Cardiac anatomical exclusions by imaging within 3 months prior to enrollment:
   a. Left atrial anteroposterior diameter ≥ 5.0 cm as documented by transthoracic echocardiography (TTE) or computed tomography (CT)
   b. Left ventricular ejection fraction ≤ 40% as documented by TTE
4. Any of the following cardiac procedures, implants or conditions:
   a. Clinically significant arrhythmias other than AF
   b. Hemodynamically significant valvular disease
   c. Prosthetic heart valve
   d. NYHA Class III or IV CHF
   e. Previous endocardial or epicardial ablation or surgery for AF
   f. Atrial or ventricular septal defect closure
   g. Atrial myxoma
   h. Left atrial appendage device or occlusion
   i. Pacemaker, ICD or CRT
   j. Significant or symptomatic hypotension
   k. Bradycardia or chronotropic incompetence
   l. History of pericarditis
   m. History of rheumatic fever
5. Any of the following within 3 months of enrollment:
   a. Myocardial infarction
   b. Unstable angina

   c. Percutaneous coronary intervention
   d. Heart surgery (e.g. coronary artery bypass grafting, ventriculotomy, atriotomy)
   e. Heart failure hospitalization
   f. Stroke or TIA
   g. Clinically significant bleeding
   h. Pericarditis or pericardial effusion
   i. Left atrial thrombus
6. History of blood clotting or bleeding abnormalities.
7. Contraindication to, or unwillingness to use, systemic anticoagulation
8. Contraindications to CT or MRI
9. Sensitivity to contrast media not controlled by premedication
10. Women of childbearing potential who are pregnant, lactating or not using birth control
11. Serious or untreated medical conditions that would prevent participation in the study, interfere with assessment or therapy, or confound data or its interpretation, including but not limited to
    a. Solid organ or hematologic transplant, or currently being evaluated for an organ transplant
    b. Severe lung disease, pulmonary hypertension, or any lung disease involving abnormal blood gases or significant dyspnea
    c. Chronic renal insufficiency of < 60 mL/min/1.73 m^2, any history of renal dialysis, or history of renal transplant
    d. Active malignancy or history of treated cancer within 24 months of enrollment
    e. Clinically significant gastrointestinal problems involving the esophagus, stomach and/or untreated acid reflux
    f. Clinically significant infection
    g. Predicted life expectancy less than one year
12. Clinically significant psychological condition that in the investigator's opinion would prohibit the subject's ability to meet the protocol requirements
13. Current or anticipated enrollment in any other clinical study
14. Body Mass Index (BMI) > 35
15. Distorted cardiac anatomy due to congenital heart disease

5.3 Study Endpoints

5.3.1 Primary Safety Endpoint

The primary safety endpoint for this study is the Composite Safety Endpoint (CSE) defined as the incidence of the following early-onset and late-onset serious adverse events (SAEs) which are device- or procedure-related:

Early onset (within 30 days of any endocardial ablation for atrial fibrillation)

- Death
- Myocardial infarction (MI)
- Persistent diaphragmatic paralysis
- Stroke or transient ischemic attack (TIA)
- Peripheral or organ thromboembolism
- Pericarditis
- Cardiac tamponade / perforation
- Vascular access complications
- Hospitalization (initial or prolonged)*
- Heart block

Late onset (any time during follow-up)

- Pulmonary vein (PV) stenosis (> 70% diameter reduction from baseline)
- Atrio-esophageal fistula

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

Table 3. Primary AE Safety Endpoint Definitions

Primary Adverse Event	Description/Criteria
Death	Death
Myocardial infarction (MI)	Myocardial infarction will be demonstrated by any one of the following: 1) detection of ECG changes indicative of new ischemia (new ST-T wave changes or new LBB) that persist for more than 1 hour. 2) development of new pathological Q waves on an ECG 3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
Persistent diaphragmatic paralysis	Change in baseline diaphragmatic function as evidenced by elevation of the diaphragm above the normal range but not due to a pulmonary process such as atelectasis.
Stroke or transient ischemic attack (TIA)	Stroke is 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 is a new focal neurological deficit with rapid symptom resolution always within 24 hours.
Peripheral or organ thromboembolism	Formation in a blood vessel of a clot (thrombus) that results from the breaking loose of all or part of an existing thrombus, which is then carried by the blood to lodge in/occlude a more distal vascular site.
Pericarditis	Inflammation of the pericardial space that results in an effusion that leads to hemodynamic compromise or required pericardiocentesis, prolongs hospitalization by more than 48 hours, requires hospitalization, or persists for more than 30 days following the ablation procedure.
Cardiac tamponade/perforation	The development of a significant pericardial effusion during or within 30 days of undergoing the index AF ablation procedure. A significant pericardial effusion is one which results in hemodynamic compromised (<80mmHg systolic bp), requires elective or urgent pericardiocentesis, or results in a 1cm or more pericardial effusion as documented by echocardiography.
Vascular access complications	Vascular access complication (e.g. groin hematoma, AV fistula, pseudoaneurysm) requiring intervention (e.g. surgical repair, blood transfusion) or admission or prolonged hospitalization.
Hospitalization (initial or prolonged)	*excludes hospitalization (initial or prolonged) solely due to arrhythmia (AF/AFL/AT) recurrence

Primary Adverse Event	Description/Criteria
	or due to non-urgent cardioversion (pharmacological or electrical)
Heart block	Impairment of AV conduction requiring intervention due to inappropriate ablation application.
Pulmonary vein (PV) stenosis	>70% diameter reduction of pulmonary vein from baseline CT/MRA scan.
Atrio-esophageal fistula	Connection between the atrium and the lumen of the esophagus as evidenced by documentation of esophageal erosion combined with evidence of a fistulous connection to the atrium.

5.3.2 Secondary Safety Endpoint

1. The proportion of subjects reporting one or more device- or procedure-related SAEs, as assessed at 30 days, 75 days, 90 days, 6 months and 12 months of follow-up.
2. The proportion of subjects with stroke or TIA through 12 months
3. The proportion of subjects with major bleeding related to anticoagulation treatment through 12 months
4. The proportion of subjects requiring cardioversion through 12 months
5. The proportion of subjects requiring an arrhythmia-related hospitalization through 12 months

5.3.3 Primary Feasibility Endpoint

The proportion of subjects that achieve Acute Procedural Success (APS) defined as the percutaneous endocardial creation of a complete, electrically isolating set of lesions around the ostia of the pulmonary veins (PVI) using the FARAPULSE Endocardial Ablation System during the first procedure, as clinically assessed by entrance and/or exit block performed ≥ 20 minutes after the last PVI lesion is made.

5.3.4 Secondary Feasibility Endpoint

1. The proportion of subjects that achieve Chronic Procedural Success (CPS) defined as persistent electrical isolation of all initially ablated pulmonary veins assessed during an electroanatomical mapping procedure performed 75 days following the index procedure. Chronic Procedural Success will be subdivided by single procedure and reablated subjects.
2. The proportion of subjects that achieve Therapeutic Success, defined as freedom from:
   a. Post blanking period through assessment: occurrence of AF, AFL or AT, or ablation for AF/AFL/AT using the study device
   b. At any time: ablation for AF/AFL/AT with a nonstudy device

Therapeutic success will be assessed from the end of the blanking period at Months 6 and 12, and will be subdivided by on / off AFDs post blanking period.

5.3.5 Additional Endpoints

1. Proportion of all ablated pulmonary veins that are isolated at the index procedure using the study device.
2. Proportion of all ablated pulmonary veins acutely isolated using the study device that remain isolated at the 75 day remapping procedure.

5.4 Sample Size

Up to 80 subjects will be enrolled in this clinical safety and feasibility study.

5.5 Investigational Sites

The clinical study will be conducted at Nemocnice Na Homolce in Prague, Czech Republic and at Hopital cardiologique du Haut-Leveque, Pessac, France.

5.6 Duration of Subject Participation

Subjects will be followed at 7 days, 30 days, 75 days, 90 days, 6 months and 12 months with a blanking period for recurrent atrial fibrillation or atrial tachycardia of 90 days following the index PEF catheter ablation procedure.

The enrollment period is estimated to take 9 months and subjects will be followed for up to 12 months for a total duration of approximately 21 months.

5.7 Written Informed Consent

All subjects must provide written Informed Consent using the Ethics Committee approved Informed Consent Form before undergoing any study related procedures. Subjects cannot be asked to sign the Informed Consent document until the study has been fully approved by the institution's EC and by the Competent Authority, if applicable, and the Sponsor or their CRO representative has received and reviewed the EC-approved Informed Consent Form. Subjects who meet the general entry criteria will be asked to sign a Patient Informed Consent form 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 consent form and discuss it with their family and physician. The subject shall be informed that his/ her participation in the clinical investigation is confidential. The Informed Consent Form must be read and understood by the subject and the subject's questions answered. The form 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 Informed Consent Form. A copy of the approved Informed Consent Form along with a copy of each patient's signed consent form 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 Patient Informed Consent Form, 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 the site.

5.8 Enrollment

Subjects that meet all of 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 Informed Consent Form.

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.

5.9 Withdrawal of Subjects

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

Subjects with an ongoing AE at the time of withdrawal should be followed on study until the clinical event has been resolved or is stable if possible.

5.10 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.

5.11 Subject Confidentiality

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. 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 case report forms. 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.

5.12 Schedule of Events and Assessments

Subjects will complete the following visits and assessments as indicated below and in **Table 4**.

5.12.1 Baseline

The following baseline data will be collected:

- Medical history
- Medication history
- Pregnancy test (if applicable)
- 12-lead ECG
- Cardiac CT or MRI
- TEE or other imaging modality for exclusion of left atrial thrombus
- NYHA Classification
- Anticoagulation Monitoring: For subjects on dabigatran, perform a PTT and, if required, a thrombin time and for subjects on warfarin, assessment of INR therapeutic levels (maintain as clinically indicated)

5.12.2 Procedure

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 Deflectable Sheath will then be prepared and advanced via guidewire to the left atrium. Commercially approved multielectrode pacing catheters will then be placed in the coronary sinus and right ventricle via conventional technique. A baseline electrophysiological assessment of pulmonary vein connection to the left atrium will be made and documented via commercially approved diagnostic catheter placement in each addressable

pulmonary vein. A baseline 3D electroanatomical map may also be made at the investigator's discretion. The diagnostic catheter will then be removed from the FARADRIVE Deflectable Sheath.

The FARAWAVE Ablation Catheter will then be prepared and advanced over the guidewire to the left atrium. The guidewire will be advanced into a target pulmonary vein, the catheter splines will be deployed 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 demonstrate placement of the catheter at the ostium. Cardiac pacing capture from the external cardiac stimulator will be obtained via connection to the coronary sinus and right ventricular pacing catheters. Once pacing capture is confirmed, ablation will be performed. 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. Ablation dose will be selected at the investigator's discretion in accordance with LBL0198.

After ablation of each addressable pulmonary vein, the FARAWAVE Ablation Catheter will be undeployed and removed. A post-ablation assessment of pulmonary vein isolation will be performed as was done pre-ablation.

For a detailed description of procedure workflow refer to LBL0193 (FARADRIVE Deflectable Sheath System), LBL0195 (FARAWAVE Endocardial Catheter Ablation System), and LBL0198 (FARASTAR Endocardial Generator System). Procedural details will be captured on the Procedural Data CRF. The following procedural data will be collected:

- Medications administered
- Pregnancy test (if applicable)
- Pre- and post-ablation 3D electroanatomical maps
- Fluoroscopic examination of diaphragm motion
- Anticoagulation monitoring (ACT for procedural monitoring)
- Adverse Events

5.12.3 Pre-Discharge and 7 Day Follow Up

Prior to hospital discharge (or 7 Day ± 2 days Follow Up) the following data will be collected:

- Medications including use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications
- Cardiac rhythm as determined by a 12-lead ECG
- Cardioversion(s)
- Heart failure status as assessed by NYHA classification

- Anticoagulation Monitoring: For subjects on anticoagulants, assessment of INR/PTT therapeutic levels as applicable/required (maintain as clinically indicated)
- Adverse Events

5.12.4 30 Day Follow-Up

Discharged subjects will return for an office visit 30 days (± 7 days) post-ablation treatment. Subjects that continue to be hospitalized 30 days post-ablation will have their 30-Day Follow-Up assessment performed at discharge. At a minimum, the following data will be collected at the 30 Day Follow-Up visit:

- Medications including 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 since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Anticoagulation Monitoring: For subjects on anticoagulants, assessment of INR/PTT therapeutic levels as applicable/required (maintain as clinically indicated)
- Any hospital readmissions, including admission and discharge dates, since discharge from the original procedure
- Adverse Events

5.12.5 75 Day Follow-Up

Subjects will return for an office visit at 75 days (± 15 days) post index ablation. At a minimum, the following data will be collected at the 75-day follow-up visit:

- Medications including use, changes in or discontinuation of anticoagulation, rate control and/or antiarrhythmic medications
- Pregnancy test (if applicable)
- Cardiac rhythm as determined by a 12-lead ECG
- Cardiac CT or MRI scan to assess the patency of the pulmonary veins
- 3D electroanatomical remapping procedure to assess electrical isolation of the pulmonary veins. Any electrical gaps may be closed at the investigator's discretion using a commercially approved ablation device. This will consist of placement of catheters in the left atrium via femoral access and transseptal puncture using conventional electrophysiology techniques. Any electrical gaps may be closed at the investigator's discretion using the study device or, if clinically necessary, using a commercially approved ablation device (which constitutes a therapeutic treatment failure).

- An Event Monitor will be provided to be used up to the 12-month follow-up visit for weekly scheduled and ad hoc symptomatic monitoring. Subjects will retain this device through the 12-month follow-up, ECG data from this monitor will be analyzed by a contract core lab. Investigational sites will be provided with the Event Monitor device and instructions for its use by the contract core lab. The investigational sites will then provide the device and instructions for use to the subject. The Event Monitor will be returned at the end of the subject's follow-up using shipping materials provided by the core lab.
- Cardioversions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Fluoroscopic Examination of Diaphragm Motion if the procedural examination indicates diminished phrenic nerve response
- Anticoagulation Monitoring: For subjects on anticoagulants, assessment of INR/PTT therapeutic levels as applicable/required (maintain as clinically indicated)
- Any additional ablation procedures performed
- Any hospital readmissions, including admission and discharge dates, since the previous visit
- Adverse Events

5.12.6 90-Day Phone Call

In case the 75-day follow-up visit and electroanatomical re-mapping procedure occur earlier than planned, the subject will be contacted by phone to collect information on any hospitalizations, repeat ablations, adverse events and/or symptoms of AF, AFL, or AT at 90 days post index procedure.

5.12.7 6 Month Follow-up

Subjects will return for an office visit 6 months (180 days ± 30 days) post-ablation treatment. At a minimum, the following data will be collected at 6 months:

- Medications including 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 rhythm as determined by a 24-hour continuous ECG monitor. ECG data from this monitor will be analyzed by a contract core lab. Investigational sites will be provided with the continuous ECG monitor device and instructions for its use by the contract core lab. The investigational sites will then provide the device and instructions for use to the subject. The device will be worn by the subject for a single 24-hour period and then returned to the core lab with shipping materials provided by the core lab.

- Event Monitor provided at the 75-day follow-up visit will be reviewed for weekly scheduled and ad hoc symptomatic monitoring. ECG data from this monitor will be analyzed by a contract core lab.
- Cardioversions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Fluoroscopic Examination of Diaphragm Motion if the procedural examination indicates diminished phrenic nerve response
- Anticoagulation Monitoring: For subjects on anticoagulants, assessment of INR/PTT therapeutic levels as applicable/required (maintain as clinically indicated)
- Any additional ablation procedures performed
- Any hospital readmissions, including admission and discharge dates, since the previous visit
- Adverse Events

5.12.8 12 Month Follow-Up

Subjects will return for an office visit 12 months (365 days ± 30 days) post-ablation treatment. At a minimum, the following data will be collected at 12 months:

- Medications including 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 rhythm as determined by a 24-hour continuous ECG monitor. ECG data from this monitor will be analyzed by a contract core lab. Investigational sites will be provided with the continuous ECG monitor device and instructions for its use by the contract core lab. The investigational sites will then provide the device and instructions for use to the subject. The device will be worn by the subject for a single 24-hour period and then returned to the core lab with shipping materials provided by the core lab.
- Event Monitor provided at the 75-day follow-up visit will be reviewed for weekly scheduled and ad hoc symptomatic monitoring. ECG data from this monitor will be analyzed by a contract core lab. The Event Monitor will be returned at the end of the subject's follow-up using shipping materials provided by the core lab.
- Cardioversions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Fluoroscopic Examination of Diaphragm Motion if the procedural examination indicates diminished phrenic nerve response

- Anticoagulation monitoring: For subjects on anticoagulants, assessment of INR/PTT therapeutic levels as applicable/required (maintain as clinically indicated)
- Any additional ablation procedures performed
- Any hospital readmissions, including admission and discharge dates, since the previous visit
- Adverse Events

5.13 Unscheduled Visit

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. At the minimum, the following data will be collected:

- Medications including 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
- Event Monitor provided at any previous follow-up visit will be reviewed for weekly scheduled and ad hoc symptomatic monitoring. ECG data from this monitor will be analyzed by a contract core lab.
- Cardioversions since last visit
- Heart failure status as assessed by NYHA classification at the time of visit
- Anticoagulation monitoring: For subjects on anticoagulants, assessment of INR/PTT therapeutic levels as applicable/required (maintain as clinically indicated)
- Any additional ablation procedures performed
- Any hospital readmissions, including admission and discharge dates, since the previous visit
- Adverse Events

5.14 Study Exit or Premature Withdrawal

Once the subject has completed the final follow-up visit they can be exited from the study provided that they do not have any conditions that require continued follow-up.

If a patient withdraws from the study prematurely or is withdrawn based on the judgement of investigator, the site will document the reason for withdrawal and inform the Sponsor. These patients will continue to be followed for safety through the 12-month timepoint.

5.15 Schedule of Study Assessments

Table 4: Summary of Study Assessments

Assessment	Baseline	Procedure	PreDischarge / 7 Days	30 Days Post-Procedure/ Discharge*	75 Days	90 Days****	6 Month	12 Month	Unscheduled
Visit Timeframe (days)			7±2	30±7	75±15	90 ±7	180±30	365±30	-
Medical History	X								
Medication History (current)	X								
Medications		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
24-Hour Continuous ECG Monitor (e.g., Holter)							X	X	
Cardiac CT or MRI	X				X				
TEE or other imaging modality (to exclude left atrial thrombus)	X								
Electroanatomical Mapping		X			X				
Event Monitor					X		X	X	X
Record DC Cardioversions at Discharge or since Last Visit			X	X	X	X****	X	X	X
NYHA Classification	X		X	X	X		X	X	X
Fluoroscopic Examination of Diaphragm Motion		X			X***		X***	X***	
Anticoagulation Monitoring	X**	X**	X**	X**	X**		X**	X**	X**
Adverse Events		X	X	X	X	X****	X	X	X
Phone Consultation						X****			

* Whichever is later
** INR or PTT (as applicable for patient on heparin or NOACs); ACT for procedural monitoring
***If the procedural study indicates decreased phrenic nerve function
****If the 75-day follow-up occurs earlier than planned; the patient will be contacted for a telephone follow-up consultation..

6. Risk Benefit Assessment

The Sponsor has conducted an analysis of the benefits and risks of the FARAPULSE Endocardial Ablation System 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.

6.1 Risks

The risk profile associated with the FARAPULSE Endocardial Ablation System 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.

6.1.1 Potential Adverse Events

The following anticipated adverse events have been identified as possible complications of percutaneous atrial fibrillation ablation procedures and these and others may be associated with the FARAPULSE Endocardial Ablation System:

- Access site complications (e.g., hematoma, pseudo-aneurysm)
- Air embolism
- 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
- Cardiac arrest or cardiac failure
- Catheter entrapment
- Cardiogenic shock
- Conduction system injury resulting in sinus arrest or heart block, either transient or permanent
- Congestive heart failure
- Death
- Drug allergic reaction or side effects (e.g., from contrast, steroids, analgesics, anesthetics, anticoagulants, sedatives, etc.)
- Esophageal injury, ulcer or fistula
- Hemorrhage
- Hemodynamic compromise
- Hemopericardium
- Hemoperitoneum

- Hemothorax
- Local infection, systemic infection, and/or sepsis
- Myocardial infarction / transient ischemia
- Nerve damage
- Organ failure
- Pain
- Perforation (e.g., of diaphragm, heart, liver, lung, and/or vessels).
- Pericardial irritation
- Pericardial effusion
- Pericarditis
- Peritonitis
- Phrenic nerve injury
- 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 or open-heart surgery to remove retained catheter
- Thrombosis
- Thromboembolism
- Vessel damage, dissection, or occlusion.

6.2 Benefits

The FARAPULSE Endocardial Ablation System is a Pulsed Electric Field (PEF) 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 Endocardial Ablation System and other commercially approved atrial fibrillation ablation systems is that the Pulsed Electric Field 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.

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.

7. Statistical Analysis and Endpoint Assessment

7.1 General Statistical Considerations

The primary objective of this study is to further characterize the safety and feasibility of the FARAPULSE Endocardial Ablation System in subjects with paroxysmal atrial fibrillation.

This is a feasibility 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.

All subjects will be followed on an Intent-to-Treat basis. The device performance will be assessed based on an intent-to-treat analysis of the primary safety and feasibility endpoints, and secondary feasibility endpoints. A per protocol analysis, along with other secondary analyses, will also be reported.

An intent-to-treat analysis of device performance will be assessed as the number of patients in whom all pulmonary veins are electrically isolated using only the study device at the completion of the index procedure.

All subjects who meet enrollment criteria for the study and undergo catheterization and ablation procedures with the FARAPULSE Endocardial Ablation System shall be included in the Intent-to-Treat cohort/population. This will exclude any patients in whom exclusion criteria were identified prior to any ablation with the study device.

Demographic, baseline clinical and disease characteristics, procedural results and primary, secondary and all additional endpoints will be summarized using descriptive statistics.

7.2 Sample Size Justification

The subject investigation is an expansion of the PEFCAT safety and feasibility study. A total of up to 80 patients will be studied at two centers to allow for continued assessment of the FARAPULSE Endocardial Ablation System and gain additional investigator experience. The subject investigation will be used to inform

the clinical dosage and procedural requirements to support a subsequent Pilot Study.

The safety and feasibility of the device will be analyzed before embarking on larger fully powered clinical studies to analyze safety and effectiveness of the FARAPULSE Endocardial Ablation System.

The sample size of up to 80 patients at two sites will allow event rate estimates for safety and device performance and associated confidence intervals. Two participating centers allow the collection of safety and feasibility data from multiple clinical users. These data will be used to inform the statistical powering of a future pilot study.

7.3 Demographic, Safety, Feasibility and Effectiveness Data

Demographic and baseline clinical and disease characteristics will be summarized in tables. For continuous variables, the summary will include number, mean, and standard deviation and 95% bilateral confidence intervals, where pertinent. Summaries for categorical variables will include the number and percent of subjects in each category.

7.4 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.

7.5 Assessment of Feasibility

7.5.1 Primary Feasibility Endpoint

The proportion of subjects that achieve Acute Procedural Success (APS) defined as the percutaneous endocardial creation of a complete, electrically isolating set of lesions around the ostia of the pulmonary veins (PVI) using the FARAPULSE Endocardial Ablation System during the first procedure, as clinically assessed by entrance and/or exit block performed ≥ 20 minutes after the last PVI lesion is made.

7.5.2 Secondary Feasibility Endpoint

1. The proportion of subjects that achieve Chronic Procedural Success (CPS) defined as persistent electrical isolation of all initially ablated pulmonary veins assessed during an electroanatomical mapping procedure performed 75 days following the index procedure. Chronic Procedural Success will be subdivided by single procedure and reablated subjects.
2. The proportion of subjects that achieve Therapeutic Success, defined as freedom from:
    a. Post blanking period through assessment: occurrence of AF, AFL or AT, or ablation for AF/AFL/AT using the study device
    b. At any time: ablation for AF/AFL/AT with a nonstudy device

Therapeutic success will be assessed from the end of the blanking period at Months 6 and 12, and will be subdivided by on / off AFDs post blanking period.

7.5.3 Additional Endpoints

1. Proportion of all ablated pulmonary veins that are isolated at the index procedure using the study device.
2. Proportion of all ablated pulmonary veins acutely isolated using the study device that remain isolated at the 75 day remapping procedure.

7.6 Assessment of Safety

7.6.1 Primary Safety Endpoint

The primary safety endpoint for this study is the Composite Safety Endpoint (CSE) defined as the incidence of the following early-onset and late-onset serious adverse events (SAEs) which are device- or procedure-related:

Early onset (within 30 days of any endocardial ablation for atrial fibrillation)

- Death
- Myocardial infarction (MI)
- Persistent diaphragmatic paralysis
- Stroke or transient ischemic attack (TIA)
- Peripheral or organ thromboembolism
- Pericarditis
- Cardiac tamponade / perforation
- Vascular access complications
- Hospitalization (initial or prolonged)*
- Heart block

Late onset (any time during follow-up)

- Pulmonary vein (PV) stenosis (> 70% diameter reduction from baseline)
- Atrio-esophageal fistula

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

7.6.2 Secondary Safety Endpoint

1. The proportion of subjects reporting one or more device- or procedure-related SAEs, as assessed at 30 days, 75 days, 6 months and 12 months of follow-up.
2. The proportion of subjects with stroke or TIA through 12 months
3. The proportion of subjects with major bleeding related to anticoagulation treatment through 12 months
4. The proportion of subjects requiring cardioversion through 12 months

5. The proportion of subjects requiring an arrhythmia-related hospitalization through 12 months

7.7 Final Clinical Report

A final clinical report will be prepared at the conclusion of the study. Copies of the final report will be provided to the investigator and their IRB/EC and to the Competent Authority, as applicable.

8. Adverse Events and Serious Adverse Events

Definitions below are as per the ISO 14155:2011

8.1 General

Adverse Event (AE):

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.

Serious Adverse Event (SAE):

- led to death,
- led to 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.
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

NOTE: 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.

Adverse Device Effect (ADE):

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

Serious Adverse Device Effect (SADE):

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event

Unanticipated Serious Adverse Device Effect (USADE):

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.

NOTE: 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.

Device Deficiency:

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.

Use Error:

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.

Malfunction:

Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or CIP.

Causality Relationship:

The investigator will assess the causality of all adverse events in relation to the research, i.e., the relationship between the AE / SAE and the investigational device or any other study-related procedures.

Each SAE will be classified 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.

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 adverse device effect (UADE). An UADE is defined as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects."

8.2 Adverse Event Reporting

All AEs, including all SAEs, will be monitored from the time of enrollment through discharge for this study. All AEs must be recorded in the patient chart and appropriate Case Report Form (CRF). 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 relationship between the AE and the study device.

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

The investigator should report to the Sponsor or its designee the following events, whether expected or not, in the corresponding CRF, with the exception of AEs / SAEs detected before the patients has signed the Informed Consent Form.

- AEs
- SAEs
- Device Deficiencies or Malfunctions that did not but might have led to a SAE if such an event were to recur:
    - Suitable action had not been taken, or
    - Intervention had not been made or
- New findings/updates in relation to already reported events.

If an AE / SAE is present at the beginning of study prior to the subject providing signed Informed Consent to participate in the study, only its worsening should be reported.

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.

This reporting should be done by faxing / emailing the completed CRF pages to the CRO and Sponsor:

CRO:	MedPass International SAS
Fax:	+33 (0)1 40 53 81 11
Sponsor:	FARAPULSE, Inc.
Email:	clinical@farapulse.com
Contact:	Mr. Christopher Schneider

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.

8.3 Device Deficiencies / 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.

8.4 Reporting to Ethics Committee / Competent Authority

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.

9. Monitoring

9.1 Study Monitoring

Clinical monitors, qualified by training and experience, will be responsible for monitoring and overseeing the conduct of the study. The clinical monitors will evaluate compliance with the protocol, any specific recommendations made by the site's Ethics Committee (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 Informed Consent Form 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 Case Report Forms (CRFs) are in agreement with the source documentation and other records. The Investigator will make available to the clinical monitor for review all Informed Consent Forms, 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 course of 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

with 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.

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 course of 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.

10. 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 Contract Research Organizations (CROs). Together, the Sponsor, consultants and CRO will ensure that the study is conducted according to the approved Clinical Investigational Plan, Ethics Committee approved Informed Consent Form 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.

10.1 Key Contributors

10.1.1 Study Sponsor

FARAPULSE, Inc.
3715 Haven Ave. Suite 110
Menlo Park, CA 94025, USA
Phone: 617-686-7661

Email: kschneider@farapulse.com

10.1.2 CRO

MedPass International SAS
95b Boulevard Pereire
75017 Paris, France
Tel No: +33 1.42.12.83.30

10.1.3 Clinical Site

The multi-center study will be conducted at the Nemocnice Na Homolce located in Prague, Czech Republic and Hopital cardiologique du Haut-Leveque in Pessac, France.

10.2 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.

10.2.1 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 Competent Authority and the local Ethics Committee. 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.

10.2.2 Ethics Review

Before any subject can be enrolled in this study, the local or national Ethics Committee and the Competent Authority (CA) must review and approve the Clinical Investigation Plan and the Informed Consent Form to be used. A subject cannot be asked to sign the Informed Consent Form until the study has been fully approved by the institution's Ethics Committee and by the CA, if applicable. The Sponsor or their designated CRO (MedPass International) will require a copy of any Ethics Committee correspondence, as well as the final Ethics Committee approval letter and the final Ethics Committee approved Informed Consent Form (ICF), and approvals for Clinical Investigation Plan and ICF revisions on amendments from the Ethics Committee. The Sponsor or their designated CRO (MedPass International) will keep all of the Competent Authority correspondence, as well as the CA approval letter.

10.2.3 Informed Consent

Subjects will not sign the Informed Consent Form until the study has been fully approved by the institution's Ethics Committee and the Sponsor or their CRO representative (MedPass International) has received and reviewed the specific Ethics Committee-approved Informed Consent Form. When the Investigator has determined the eligibility of a specific subject to enter the study, the Informed Consent Form must be completed. The Informed Consent Form 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 Informed Consent Form.

10.2.4 Coverage of Expenses

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

10.2.5 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 representative (MedPass International), Investigators and Site personnel will make every reasonable effort to protect the confidentiality of all subjects participating in the study.

10.3 Insurance

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

10.4 Audits and Inspections

The Principal Investigator will also allow representatives of the governing Ethics Committee (EC), Competent Authority (CA), the U.S. Food and Drug Administration (FDA), 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 Clinical Investigation Plan, completeness and exactness of the data being entered onto the CRFs and compliance with FDA or other regulatory agency regulations.

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

10.5 Sponsor Responsibilities

Sponsor has the overall responsibility for the study and will:

- Select qualified Principal Investigator, clinical investigators and study site.
- Select qualified monitors.
- Provide the Clinical Investigation Plan and any subsequent amendments.

- Provide appropriate information and Investigational system training to the Investigator and study site staff.
- Ensure that all deviations from the Clinical Investigation Plan 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 adverse events and all adverse device effects (ADEs) are reported and reviewed with the Investigator(s), and where appropriate, that all serious adverse events (SAEs) and all serious adverse device effects (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 Endocardial Ablation System Instructions for Use, the Clinical Investigation Plan, CRF instructions, CRFs and requirements for obtaining informed consent.
- Provide the FARAPULSE Endocardial Ablation System to the participating study site, in quantities to support study activities.
- Coordinate ongoing communication with CRO(s), 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 binder to site.

10.6 Monitor Responsibilities

The Sponsor has contracted MedPass International as the Clinical Monitor to support the Sponsor in implementing and monitoring the clinical investigation until its termination. Clinical monitors, qualified by training and experience, will be responsible for monitoring and overseeing the conduct of the study.

Site Initiation Visit: 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 Informed Consent Form, the CRFs, CRF Instructions, 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 to evaluate compliance with the Clinical Investigation Plan (CIP), any specific recommendations made by the site's Ethics Committee (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 Form was properly obtained 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 Case Report Forms (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 Informed Consent Forms, 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 close out visit will be conducted to ensure that all data collection and study requirements are complete.

10.7 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 (CTA)
- 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 Clinical Investigation Plan, 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 Clinical Investigation Plan (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 Ethics Committee and Competent Authority 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 Ethics Committee Informed Consent Form.
- 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.

10.8 Investigator Training

The participating investigator will be trained in the use of the FARAPULSE Endocardial Ablation System 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.

10.9 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 Clinical Investigation Plan, 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.

10.10 Clinical Events Committee and Data and Safety Monitoring Board

A Clinical Events Committee (CEC) will convene during the study to classify and adjudicate all procedure-related and serious adverse events reported in the subject investigation. The CEC will consist of physicians who have no formal involvement or conflict of interest with the subjects, the investigator, or the designated CRO (MedPass International), and will be appointed by the Sponsor. The CEC will be provided with case summaries and relevant source documents in order to adjudicate the adverse events.

In addition, a Data and Safety Monitoring Board (DSMB) will convene to review safety data and trends during the conduct of the study. The DSMB will meet, at a minimum, after the enrollment of every twentieth (20^{th}) patient until the conclusion of enrollment up to a total of 80 patients. The DSMB will be empowered to terminate or pause the study if it identifies a trend that indicates a danger to patient safety. In particular, the DSMB will consider safety trends in the context of different versions of the device (e.g. 35mm vs. 31mm FARAWAVE Endocardial Ablation Catheters).

10.11 Data Management

Patient Case Report Forms (CRFs) will be provided to the participating site. Investigators are responsible for the accurate completion of patient CRFs during the study. The Investigator will ensure that complete, accurate and timely data on CRFs 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 Clinical Investigation Plan, including laboratory results, supporting medical records, and signed Informed Consent Forms. The source documents will be used during the regular monitoring visits to verify information from the database against data contained on the completed CRFs.

After CRF Monitoring has been complete and deficiencies / discrepancies resolved, CRFs will be provided to the Sponsor or CRO, and data from the study will be entered from the CRFs into a central database. CRF 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 (MedPass International).

10.12 Study Suspension or Early Termination

The study can be discontinued 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 Endocardial Ablation System making treatment without the FARAPULSE Endocardial Ablation System 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.

10.13 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 Case Report Forms prior to scheduled monitoring visits;
- Failure to obtain written Informed Consent;
- Failure to report SAEs/ UADEs to Sponsor within 24 hours of knowledge;
- Loss of (or unaccounted for) investigational product inventory or repeated failure of device accountability.

10.14 Final Clinical Report

A Final Clinical Report will be prepared even if the study is prematurely terminated. The Final Clinical Report will be submitted to the participating Investigator, and regulatory agencies, as required.

10.15 Deviations from the Clinical Investigation Plan

The Investigator is not allowed to deviate from the approved Clinical Investigation Plan except in emergency circumstances.

The Investigator must notify the Sponsor and the CRO of any deviation from the Clinical Investigation Plan and document the reason for the deviation.

The Investigator shall notify the Sponsor and the reviewing Ethics Committee of any deviation from the Clinical Investigation Plan, 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.

11.Regulatory considerations

11.1 Maintaining Records

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

11.2 Data Handling and Record Keeping

11.2.1 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.

11.2.2 Data Collection

The Investigator must maintain detailed records on all subjects who sign the Informed Consent Form and begin the pre-procedure evaluation. Data for enrolled subjects is transcribed onto CRFs provided by the Sponsor or designee. All data should be transcribed completely, promptly and legibly. Corrections should be made in a manner that does not obscure or eliminate the original error, by striking through the original data with one line, and initialing and dating the change, along with the reason for the change (if not obvious). Original CRF pages will be collected by the Sponsor or Sponsor's designee after they are reviewed by the study monitor. The investigator should maintain a copy of all completed CRFs from this study.

Study exit forms will be completed for all enrolled subjects, regardless if 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.

11.3 Ethics Committee (EC) and Competent Authority (CA) Approval

Regulatory approvals must be obtained prior to enrolment 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 Ethics Committee and Competent Authority correspondence, as well as the final approval letter from the Ethics Committee and Competent Authority, where applicable.

An Investigator may not make Clinical Investigation Plan (CIP) changes without prior approval by the Sponsor. All significant (CIP) changes that may affect the following must be submitted and approved by the Ethics Committee and Competent Authority 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.

11.4 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.

12. 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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