CathVision

THE AUTOMATED CALCULATION OF AF CYCLE LENGTH AND COMPLEXITY USING A NOVEL EP RECORDING SYSTEM (CATHVISION ECGENIUS® SYSTEM).

CLINICAL INVESTIGATION PLAN (CIP)

INVESTIGATIONAL PRODUCT:	CATHVISION ECGENIUS® SYSTEM
PROTOCOL NUMBER:	CVAR-00002-A
DATE:	24 AUGUST 2022
CLINICALTRIALS.GOV NUMBER:	**NCT05477602**

ADMINISTRATIVE INFORMATION

CONTACTS:

Medical, Clinical, and Operational Support

Sponsor Name:	CathVision ApS
Sponsor Telephone Number	+45 61 30 50 61
Manufacturer and Sponsor Address:	CathVision ApS Titangade 11 2200 Copenhagen N Denmark

AMENDMENT HISTORY:

Date	Amendment Number	Amendment Type
24 Aug 2022	Original	Original protocol, version 1.0

SPONSOR PROTOCOL APPROVAL

Representatives of CathVision ApS

This study will be conducted with the highest respect for the individual participants in accordance with the requirements of this clinical study protocol and in accordance with the following:

- The ethical principles that have their origin in the Declaration of Helsinki.
- International Conference on Harmonized Tripartite Guideline for Good Clinical Practice E6 (ICH GCP E6).
- All applicable laws and regulations, including, without limitation, data privacy laws and regulations.

SIGNATURES

Approver		
Signature	**Location**	**Date**
	CathVision ApS	
Name: Mads Emil Matthiesen		dd-Mmm-yyyy
CEO		
Reviewer		
	AKRN Scientific Consulting	
Name:		dd-Mmm-yyyy
Author		
	CathVision ApS	
Name: Karl Firth		dd-Mmm-yyyy
Clinical Research Manager		

INVESTIGATOR'S AGREEMENT

I have read this Clinical Investigation Protocol. I will provide copies of this Clinical Investigation Protocol and all pertinent information to all site personnel involved in this study. I will discuss this material with them and ensure they are fully informed regarding the study products and the conduct of the study.

I agree to conduct the study as outlined in the Clinical Investigation Protocol and in accordance with the signed clinical study agreement.

I will obtain written informed consent from all participating subjects/patients in accordance with requirements as specified in ICH Guidelines for Good Clinical Practice; Section 4.8 and I will fulfill all responsibilities for submitting pertinent information to the EC. I will use only the informed consent form approved by the sponsor and the Ethics Committee (EC) or it's representative.

I understand that this study will not be initiated without the approval of the Ethics Committee and that all administrative requirements of the governing body of the institution will be complied with fully.

I also agree to report all information or data in accordance with the protocol and I agree to report without unjustified delay, all Adverse Events (AEs), and Serious Adverse Events (SAEs) that could have led to Unanticipated Adverse Device Events (UADEs).

I agree to provide all the information requested in the Case Report Forms presented to me by the Sponsor in a manner to assure completeness, legibility, and accuracy.

I also agree that all information provided to me by the Sponsor, including pre-clinical data, protocols, Case Report Forms, and any verbal and written information, will be kept strictly confidential and confined to the clinical personnel involved in conducting the study.

In addition, no reports or information about the study or its progress will be provided to anyone not involved in the study other than the Sponsor, the EC, and regulatory authorities (if applicable). Any such submission will indicate that the material is confidential.

I agree to have control over all clinical supplies and the investigational product provided by CathVision. I further agree not to originate or use the name of CathVision ApS and/or ECGenius® System, or any of its employees, in any publicity, news release or other public announcements, written or oral, whether to the public, press or otherwise, relating to this protocol, to any amendment hereto, or the performance hereunder, without the prior written consent of CathVision ApS.

I herewith declare that I agree with the protocol described in detail in this document and agree to conduct the study in accordance with the protocol and compliance with Good Clinical Practice and all applicable regulatory requirements.

INVESTIGATOR SIGNATURE

Signature	**Location**	**Date**
Name:		dd-Mmm-yyyy
Title:		

PROTOCOL SYNOPSIS

Title	The automated calculation of AF cycle length and complexity using a novel EP recording system (CathVision ECGenius® System).
Investigational Device	CathVision ECGenius® System
Objective	Collect electrophysiological data during atrial fibrillation (AF) ablation procedures to assess the performance of a Signal Complexity Visualization algorithm, designed to be integrated into the CathVision ECGenius® System at a later stage.
Study Design	A prospective, single-center, feasibility study using the CathVision ECGenius® system and a Signal Complexity Visualization Algorithm during radiofrequency (RF) ablation procedures to treat persistent AF. Subjects with persistent AF who are indicated to undergo a routine-practice RF ablation may be enrolled in the Study. Intracardiac signals will be passively recorded using the investigational CathVision ECGenius® System in parallel with the commercial (CE Approved) EP recording system used as standard of care at the investigational site. The investigational device will not be used for direct clinical care decisions or therapy. The validation of the Signal Complexity Visualization Algorithm will be performed offline and retrospectively.
Sample Size	A minimum of 15 and up to 30 subjects may be enrolled in this study
Investigational Site	OLV Cardiovascular Centre, Aalst, Belgium
Study Duration / Follow-up Period	Study enrollment is planned from October 2022 to December 2022. Subjects will be followed until discharged from the hospital. There is no additional study follow-up planned.
Primary Endpoint	Assessment of the performance of a Signal Complexity Visualization Algorithm for analyzing AF response to ablation, evaluated as the technical success of the CathVision ECGenius® System to collect and record intracardiac signals during routine EP procedures.
Safety Endpoint	Evaluation of adverse events and/or device deficiencies reported with the use of the CathVision ECGenius® System during the procedure until discharge.

Enrollment Criteria	Inclusion Criteria Eligible subjects must meet all of the following inclusion criteria: 1. Subjects undergoing RF ablation indicated by the investigator for the treatment of persistent atrial fibrillation. 2. At least 21 years of age. 3. Able and willing to provide written informed consent prior to any clinical investigation related procedure. Exclusion Criteria Eligible subjects must not meet any of the following exclusion criteria: 1. Current participation in another investigational drug or device study that interferes with this study. 2. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results. 3. Life expectancy less than 12 month, in the opinion of the Investigator. 4. Subjects who, in the opinion of the investigator, are not candidates for this study. 5. Subjects who, in the opinion of the investigator, are considered part of any vulnerable population.

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ABBREVIATIONS

ADE	Adverse Device Effect
AE	Adverse Event
AF	Atrial Fibrillation
AFCL	Atrial Fibrillation Cycle Length
CPK	Creatinine Phosphokinase
CS	Clinically Significant
CVA	Cerebrovascular Accident
EC	Ethics Committee
ECG/EKG	Electrocardiogram
EGM	Electrogram
EP	Electrophysiology
EPAMP	Electrophysiology Amplifier
GCP	Good Clinical Practices
ICH	International Council for Harmonisation
LV	Left Ventricular
NCS	Not Clinically Significant
PI	Principal Investigator
PV	Pulmonary Vein
RF	Radiofrequency
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SID	Subject Identification Number
TIA	Transient Ischemic Attack
TEE	Transesophageal Echocardiogram
TTM	Transtelephonic Monitoring
UADE	Unanticipated Adverse Device Effect

1. INTRODUCTION

1.1 CARDIAC ELECTROPHYSIOLOGY

Of the total worldwide population, 1% and 2% of rural and urban areas suffer from cardiac arrhythmia, respectively. Approximately 15% of patients do not respond to drug treatment and need a device-based interventional treatment. As a result, there is a large and growing need for cardiac arrhythmia ablation. Today, however, precise identification of the mechanism of the arrhythmia and subsequent successful ablation treatment is challenging for physicians. The three most prevalent arrhythmias ("complex arrhythmias") for catheter ablation are atrial fibrillation, atrial tachycardia, and ventricular tachycardia.[1]

1.2 INTRACARDIAC ELECTROPHYSIOLOGY SIGNALS

Cardiac electrograms are generated by the potential (voltage) differences recorded at two recording electrodes during the cardiac cycle. All clinical electrogram recordings are differential recordings from one source that is connected to the anodal (positive) input of the recording amplifier and a second source that is connected to the cathodal (negative) input. Unipolar recordings are obtained by positioning the exploring electrode in the heart and the second electrode (referred to as an indifferent electrode) distant (theoretically an infinite distance) from the heart such that it has little or no cardiac signal.

Bipolar recordings are obtained by connecting two nearby electrodes that are exploring the area of interest to the recording amplifier. The recorded signal is the potential difference from the positive input to the negative input. Because a signal from a far-field source will present a common potential to the two electrodes, it is largely subtracted out, leaving the local signal. In a homogeneous sheet of tissue, the initial peak of the bipolar signal coincides with depolarization beneath the recording electrode[2].

Cardiac arrhythmias can be mapped by measuring the cardiac electrograms at relevant anatomical locations, such as within the left atrium for atrial fibrillation.

1.3 RATIONALE FOR THIS CLINICAL INVESTIGATION

Paroxysmal atrial fibrillation (AF) is characterized by episodes of chaotic atrial activation that are shorter than seven days in length and self-terminate without interventions such as drug therapy or electrical cardioversion.[1] For paroxysmal AF patients who do not respond to anti-arrhythmic drug therapy, a pulmonary vein isolation (PVI) may be indicated for symptom relief.[1]

Persistent AF is diagnosed when patients have episodes of AF lasting longer than seven days or require intervention to terminate the arrhythmia.[1] The persistent AF patient group is highly heterogeneous and ranges from patients with only short episodes of AF who are very symptomatic and seek medical attention often leading to cardioversion; to patients who have been in AF for several years under the care of a primary care physician. Whilst the guidelines for ablation of patients in paroxysmal AF clearly indicate PVI employing radiofrequency (RF) guided by a 3D mapping system, or cryo or laser balloon ablation, it is widely thought that PVI alone is not an adequate treatment for many persistent AF patients.[3] Ablation strategies in addition to PVI range from: targeting areas of low amplitude electrograms, which may indicate areas of disease;[4] mapping and ablation of areas exhibiting complex fractionated waveforms;[5] mapping and ablation of areas

displaying rotating activation;[6] mapping and ablation of unipolar electrograms with a qS morphology revealing a focal source driver;[7] linear ablation strategies to create lines of block between anatomical structures;[8] or even combinations of these approaches.[8]

Whilst many of these approaches have shown promise in improving outcomes for persistent AF patients, particularly when compared to PVI alone, the operator often has very little indication of the impact the ablation strategy is having on the underlying rhythm during the procedure. Signal features derived from the atrial electrogram during AF may be used to describe the fibrillation rhythm. As an example, the cycle length of AF (AFCL) is indicative of atrial refractoriness and can be calculated from atrial electrograms using signal processing techniques. Studies using off-line, post-procedure, retrospective processing techniques have shown that ablation may lead to a lengthening of AFCL as a precursor to reversion to sinus rhythm.[9] Indeed, such signal features may be derived from both the time (cycle length) and frequency (dominant frequency) domains. Analysis in the frequency domain has previously been used to create an index of the complexity of AF. Spectral analysis of the signal using fast Fourier transform techniques identifies the power of the dominant frequency and compares this to the total power of the signal. The greater the power of the dominant frequency, the less complex the signal.[10]

CathVision has developed an algorithm that derives features from the ECG and intracardiac electrogram signals and returns analytical information in the form of signal complexity and cycle length to the operator. In this way, the operator will be able to assess the impact of their ablation procedure.

2. DEVICE DESCRIPTION

The CathVision ECGenius® System is an investigational electrophysiology (EP) recording system to be used in EP procedures as a tool to monitor, display, and record signals of the heart and cardiac arrhythmias. The investigational device ECGenius® System includes the following items:

- Cube® EP amplifier (EPAMP)
- Pin box cable assembly for connection of catheters
- Surface ECG cable
- Data cable to host computer
- Recording system software (RECORDER SW)
- Host computer (Cube PC) and monitors

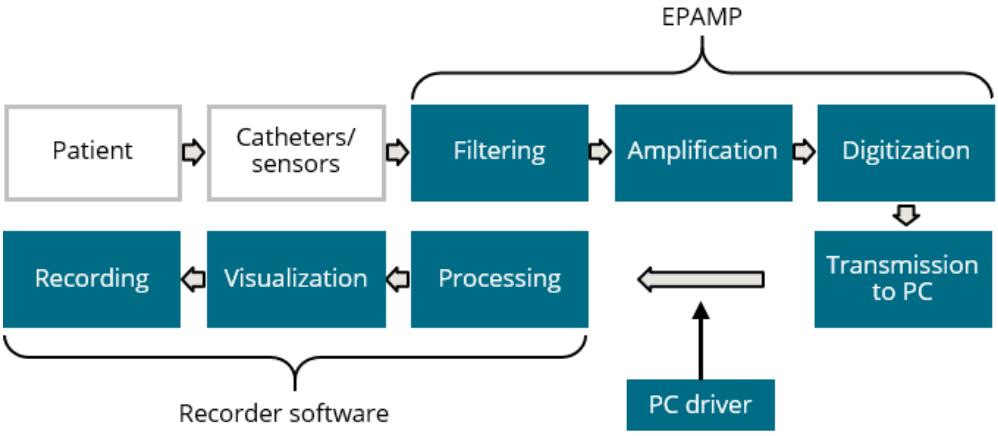
The Signal Complexity Visualization Algorithm will be used in this study to assess AF cycle length and complexity after the procedure, in an offline and retrospective manner.

Additional information regarding the device and its components, including all pre-clinical and clinical test results, can be found in the Investigator's Brochure or in the Instructions for Use.

2.1 SIGNAL PROCESSING OVERVIEW

The main hardware of the ECGenius® System is the amplifier or Cube® EPAMP, which acquires signals from third-party catheters and sensors connected to the patient. It then sends the signals to the ECGenius® PC, which has a software program called the RECORDER SW that visualizes the

signals to the user and provides the users a way to interactively analyze them. The following figure illustrates this signal pathway.



There are no parts of the medical device that may come into contact with the subject's body or body fluids. There are no medicinal products, human or animal tissues or their derivatives, or other biologically active substances used in the device.

Each manufacturing lot of investigational device part is assigned a unique lot number that is printed on the device package labeling, providing a means of traceability. A device accountability log will be used to track the use of devices in the study. The lot number will be recorded in each case report form.

The CathVision ECGenius® System will be labeled "for investigational use only."

2.2 INTENDED PURPOSE

The ECGenius System is an electrophysiology measurement system used to acquire, filter, digitize, amplify, display, and record clinical data obtained during electrophysiological studies and related procedures. The system is compatible with a 3rd-party stimulator, intended to be used for diagnostic cardiac stimulation during electrophysiological testing of the heart. The ECGenius is not intended for use with flammable gases or liquids. No part of it is sterile or sterilizable and the device is protected from ingress of fluids (IPX1).

The ECGenius is designed for use in air-conditioned hospital EP laboratories and operating rooms equipped for advanced cardiac resuscitation.

The intended users are licensed healthcare professionals (e.g. electrophysiologists), technicians and nurses working in EP laboratories and operating rooms. Typically, a technician operates the ECGenius System and a practitioner interprets the data. The nurses play a secondary role as they assist the practitioner and technician.

The intended patients are adult patients diagnosed with cardiac arrhythmia, including patients with supraventricular tachycardia and ventricular tachycardia.

3. RISK-BENEFIT ANALYSIS

The clinical investigation has been designed to involve as little pain, discomfort, fear, and any other foreseeable risk as possible for subjects. There are no known risks to the potentially enrolled subjects specifically associated with the use of the ECGenius® System, since this investigational device will passively record EP signals in parallel to a commercial and standard of care EP recording system, thus not impacting any clinical procedures.

Potential study risks include product failures similar to commercially available EP recording systems, with a similar likelihood of occurrence.

Risks associated with cardiac electrophysiology procedures include events reported in the literature related to catheter procedures, identified in the risk and hazard analyses, and associated with percutaneous interventions. A list of anticipated adverse events are defined in Section 6.5. Each adverse event and/or device effect will be evaluated in detail as described in Section 6 of this Clinical Investigation Plan (CIP).

The study is designed for parallel data collection during an electrophysiology study. The investigator diagnostic decisions will be guided by an approved EP recording system as per institution standard of care. Due to the protocol design and noninvasive nature of the tested medical device the rate of expected occurrence of SAEs or SADEs related to the use of the investigational device is low.

CathVision personnel will be responsible for the installation of the investigational device. During the study, the device will be operated by study trained site personnel.

As the treatment will be guided by an approved EP recording system, the reduction in symptomatic arrhythmia will be similar to the benefit of currently available EP recording systems.

4. INVESTIGATIONAL PLAN

4.1 STUDY OBJECTIVES

The primary objective of the study is to validate a Signal Complexity Visualization algorithm with a novel EP recording system (CathVision ECGenius® System) for the assessment of measurable changes to rhythm during persistent AF ablation procedures.

The safety of the CathVision ECGenius® System will be evaluated through adverse events and/or device deficiencies reported during the procedure until discharge.

4.2 STUDY DESIGN

This is a prospective, single-center, feasibility study using the CathVision ECGenius® system and a Signal Complexity Visualization Algorithm during radiofrequency (RF) ablation procedures to treat persistent AF.

Subjects with persistent atrial fibrillation who are indicated to undergo an RF ablation may be enrolled in the Study. Intracardiac signals will be passively recorded using the investigational

ECGenius® System in parallel with the commercial (CE Approved) CardioLab, GE EP recording system. The investigational device will not be used for direct clinical care decisions or therapy. The validation of the signal complexity algorithm will be performed offline.
A summary of the schedules of evaluations and visits can be found in section 4.7.1.

4.3 STUDY DURATION

Study enrollment is planned for 1-3 months between October and December 2022.

Subjects will be followed until discharged from the hospital, regardless of the duration of hospitalization. After the EP procedure, the estimated number of days of hospitalization is 1-2. There is no additional study follow-up planned.

4.4 SUBJECT POPULATION

A minimum of 15 and up to 30 subjects will be enrolled in the study at the investigational site.

Eligible subjects must meet the inclusion and exclusion criteria described in Sections 4.4.1 and 4.4.2 to be enrolled in the study and undergo an EP procedure using the CathVision ECGenius® System in parallel to the commercial EP system.

4.4.1 INCLUSION CRITERIA

Subjects must meet all of the following inclusion criteria to be included in the study:

1. Subjects undergoing ablation indicated by investigator for the treatment of persistent atrial fibrillation.
2. At least 21 years of age.
3. Able and willing to provide written informed consent prior to any clinical investigation related procedure.

4.4.2 EXCLUSION CRITERIA

Subjects will not be eligible for the study if any of the following exclusion criteria are met:

1. Current participation in another investigational drug or device study that interferes with this study.
2. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.
3. Life expectancy less than 12 month, in the opinion of the Investigator.
4. Subjects who, in the opinion of the investigator, are not candidates for this study.
5. Subjects who, in the opinion of the investigator, are considered part of any vulnerable population.

4.4.3 POINT OF ENROLLMENT

A subject is considered enrolled in the clinical investigation from the moment the patient provides written informed consent, has been confirmed to meet all inclusion criteria and none of the exclusion criteria, and has undergone initiation of the treatment procedure.

4.5 STUDY ENDPOINTS

4.5.1 PRIMARY ENDPOINT

The Primary endpoint of the study will be evaluated as the technical success* of CathVision ECGenius® System to collect and record intracardiac signals during routine EP procedures. Specifically:

- To extract and quantify atrial fibrillation electrogram features from the CS catheter.
- To visualize changes and label events during the procedure in relation to RF ablation delivery.

*The Signal Complexity Visualization Algorithm relies on local activation time (LAT) detection. An error in LAT annotation will produce a "no result". Technical success is defined as data of sufficient quality (low noise, detectability of LATs) for the algorithm to produce a result.

4.5.2 SAFETY ENDPOINT

The safety endpoint of this study consists of the evaluation of adverse events and/or device deficiencies reported with the use of the CathVision ECGenius® System during the procedure until discharge.

The detailed methods to analyze the primary and safety endpoints will be included in the Statistical Analysis Plan (SAP).

4.6 STUDY PROCEDURES

The following is a detailed list of study visits and the required procedures/tests per visit. Specific procedures/tests are described in Section 5.

4.6.1 INFORMED CONSENT

Pre-screening, i.e., medical record review without obtaining informed consent, is allowed.

Prior to enrollment of any subjects into the study, written approval of the protocol and informed consent must be obtained from the Ethics Committee (EC).

Informed consent will be obtained as outlined in the EU Regulation 2017/745, ISO14155:2020 and local legislation.

A research study member at the EC approved study site will speak with the study candidate about the purpose of the study and investigational research. Explanation of the study background, study

procedures, visits, assessments, risks, and benefits will be reviewed in detail with the potential subject. Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

The potentially enrolled subject will be given the time they need to read through the study information and informed consent document and ask as many questions as necessary to make them comfortable with the study and the requirements. The subject shall be provided with the Informed Consent form written in a language that is understandable to the subject and has been approved by the EC. After informed consent is obtained, study assessments may begin.

After informed consent is obtained, the study eligibility criteria are verified. All patients who signed a consent form are considered study subjects. A patient is considered enrolled after the patient has signed the informed consent form and after the inclusion/exclusion criteria have been met.

The original informed consent form will be retained with the subject records. A copy of the informed consent will be provided to the subject or legal representative.

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

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

4.6.2 SUBJECT IDENTIFICATION

To maintain confidentiality, the subject's name will not be recorded on any study document other than the informed consent form. Each enrolled subject will be assigned a study specific Subject Identification Number (SID) to be assigned in consecutive order in the following format: CVAR00002-OLVYYY. CVAR00002 is the study number, OLV is the site identifier, and YYY is the 3-digit sequential subject ID number starting with 001. For example, the first subject at the site will be assigned CVAR00002-OLV001. Subject ID numbers will not be re-used (e.g., if the subject is determined to be a screen failure).

4.7 STUDY VISITS

This section contains a detailed list of visits, from screening to discharge, and the required procedures/tests for each of them.

4.7.1 SCHEDULE OF ASSESSMENTS

	Screening	Index Procedure	Discharge
Visit Number	**1**	**2**	**3**
Informed Consent	✓		
Demographics	✓		
Cardiac History	✓		
Cardiac Anti-Arrhythmia Medications	✓		
Inclusion/Exclusion	✓		
12 lead EKG	✓		
EP procedure		✓	
Adverse Events		✓	✓
Device Deficiencies		✓	✓
Protocol Deviations	✓	✓	✓

4.7.2 VISIT 1: DAY –15 ± 15 (SCREENING VISIT)

Screening will be completed within 30 days of the index ablation procedure.

Test results from routinely performed standard assessments may be used to determine eligibility. Preliminary screening will consist of a review of relevant cardiac history, including duration and frequency of arrhythmia(s), their subsequent treatments (e.g., medications, previous ablation), and associated symptoms.

Eligibility will be assessed sequentially, starting with the least invasive and least expensive tests as follows. Results from each test or screening activity should be reviewed prior to proceeding to the next step.

- Demographics
- Baseline cardiac history
- Arrhythmia history (Type of arrhythmia, TTM, EKG, Holter, etc.)
- Baseline cardiac anti-arrhythmia medications
- 12-lead EKG

4.7.2.1 SCREEN FAILURES

Subjects not meeting all study entry criteria will be designated as screen failures. End of study procedures will not be performed for these subjects, but their reason for ineligibility will be recorded on the Screening Log. Screen failures after the screening visit are not counted towards total study enrollment.

4.7.3 VISIT 2: DAY 0 (INDEX PROCEDURE)

During the index EP procedure, institutional standard of care is to be utilized to treat the subject.

When the subject is connected to the standard EP recording system, during manipulation of catheters or diagnostic tests, intracardiac signals will be recorded using the investigational device in parallel.

The total procedure time is not expected to differ by adding the CathVision ECGenius® system to the EP system as data analysis will occur post procedure. Procedure data will be collected in the Index Procedure Case Report Form (CRF); Adverse Events and Device Deficiencies will be reported through their corresponding CRFs.

4.7.4 VISIT 3: DISCHARGE (NO SPECIFIED WINDOW)

Prior to discharge, the following will be documented:

- Adverse events
- CathVision ECGenius® device deficiencies
- Protocol deviations, if any

Subjects will be considered to have completed all study assessments and will exit the study after this visit.

4.8 STUDY COMPLETION

4.8.1 COMPLETED SUBJECTS

Subjects will be considered complete when all assessments through the Discharge have been performed in accordance with the protocol. There will be no additional clinical follow up requirements for this study.

4.8.2 DISCONTINUED SUBJECTS

Subjects may withdraw consent at any time throughout the course of the study. The investigator may discontinue a subject from the study at any time if they consider that remaining in the study compromises the subject's health or the subject is not sufficiently cooperative. In either event, reason(s) for discontinuation should be documented appropriately.

Possible reasons for study discontinuation include the following:

- Adverse events (AEs) necessitating discontinuation from the study.
- Subject decision (to be specified if possible).
- Investigator decision (to be specified).
- Other reason (to be specified).

The reasons for any subject discontinuation will be documented on the study completion form of the study CRF. If possible, subjects who withdraw before study completion will complete the reporting of data as best possible, at minimum AE assessment and CathVision ECGenius® System device deficiency, if applicable.

4.8.3 PREMATURE STUDY TERMINATION

The Sponsor, Investigator, Competent Authority (CA) or Ethics Committee (EC) have the right to suspend or terminate the study prematurely for any safety, ethical, or administrative reason at any time.

The study will be suspended or prematurely terminated if, in the opinion of the Sponsor, investigator or reviewing EC or CA, the safety of patients and/or data is uncertain. The sponsor should make

sure that the suspension or premature termination will be communicated to the PI and reviewing EC and CA.

CathVision reserves the right to suspend/terminate the investigational site from the study for any of the following reasons:

- Failure to obtain written Informed Consent
- Investigator failure to comply with training or Instructions for Use
- Failure to report SAEs/SADEs/UADEs to Sponsor within 24 hours of knowledge
- Loss of (or unaccounted for) investigational product inventory
- Repeated protocol violations
- Repeated failure to complete case report forms prior to scheduled monitoring visits

In the event of termination of investigator participation, all study-related devices and equipment, as applicable, will be returned to Sponsor.

The decision to resume study enrollment and treatment at the site will be made by the Sponsor. Additionally, the triggering of the stopping/re-activation will promptly be submitted to the involved reviewing EC for approval.

In case of study termination, patients enrolled in the study would be treated and monitored per standard of care and best clinical practices at the investigator's discretion.

4.9 INVESTIGATIONAL DEVICE ACCOUNTABILITY

Documentation of receipt, use, and return of the CathVision ECGenius® System and its parts must be maintained by the Principal Investigator (PI) or his/her designee in a device accountability log. Investigational devices are to be used only in accordance with this protocol and under supervision of the PI or a duly designated person. It is the PI's responsibility to ensure that all study devices are kept in a secure location, with access limited to individuals authorized by the investigator. A record of all study devices (by their lot or serial numbers) received, used, and returned must be maintained by the site until the conclusion of the study. Following accountability of the study devices by the Sponsor or its designee, all study devices will be returned to the Sponsor/Designee as directed in writing by the Sponsor or designee.

5. EXAMINATIONS AND EVALUATIONS

5.1 DEMOGRAPHICS

Subject demographical data, such as date of birth, gender, , height, and weight will be recorded.

5.2 CARDIAC HISTORY

Relevant cardiac history including duration and frequency of arrhythmia(s), their subsequent treatments (e.g., medications, previous ablation) and associated symptoms will be obtained at Screening. All positive and negative findings will be carefully documented. Any new finding discovered during the Screening evaluation and prior to the index ablation procedure will be considered to be part of the cardiac history and will not be recorded as an AE.

5.3 CARDIAC MEDICATIONS

Cardiac anti-arrhythmia medications will be recorded at screening visit, and medications prescribed during the index procedure visit. For each medication, the following information will be collected:

- Medication trade or generic name
- Indication for which the medication was given
- Dose/strength, route, and frequency of administration
- Date started
- Date stopped (or continuation at study completion)

5.4 12 LEAD EKG

A 12-lead electrocardiogram (EKG) will be conducted. The EKG recording will be printed out and will be placed with subject records. A copy of the EKG recording, and report summary will be made available for the study and filed with the subject study records. Any clinically significant abnormalities will be documented.

6. REPORTING OF ADVERSE EVENTS AND DEVICE DEFICIENCIES

6.1 ADVERSE EVENTS DEFINITIONS

An **adverse event (AE)** is any untoward medical occurrence, unintended disease or injury, or the deterioration of a pre-existing medical condition following or during exposure to an investigational medical device, whether or not considered causally related to the investigational medical device.

An untoward medical condition can be symptoms (e.g., nausea, chest pain), signs (e.g., tachycardia, enlarged liver), or clinically significant abnormal results of an investigation (e.g., laboratory findings, electrocardiogram).

A **serious adverse event (SAE)** is any AE which led to any of the following:

- Death,
- Serious deterioration in the subject's health as defined by one or more of the following:
    - a life-threatening illness or injury, or
    - a permanent impairment of a body structure or a body function including chronic diseases, 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.
- life-threatening fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment

Additionally, important medical events that may not result in death, be life-threatening or require hospitalization may be considered SAEs when they jeopardize the subject or require medical or surgical intervention to prevent one of the serious outcomes listed above.

Planned hospitalization for a pre-existing condition, or a procedure required by this CIP, without serious deterioration in health, is not considered a SAE.

Adverse device effect (ADE) is an AE related to the use of an investigational medical device. Note, this definition includes AEs resulting from insufficient or inadequate instructions for use, operation, or any malfunction of the investigational medical device. In addition, this definition includes any event resulting from use error or intentional misuse of the investigational medical device.

Serious adverse device effect (SADE) is an ADE that has resulted in any of the consequences characteristic of an SAE.

An **unanticipated adverse device effect** (**UADE**) is defined as any serious adverse effect on health, safety, any life-threatening problem, 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 predicate devices, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

6.2 ASSESSMENT OF ADVERSE EVENTS

The need to identify and report AEs is not dependent upon whether or not the clinical event is associated with the use of the study device or procedure. All AEs, regardless of severity, occurring at the index ablation through study completion visit must be recorded in the corresponding CRF. Events occurring prior to the EP procedure must be listed in the cardiac history.

Any Adverse Event(s) that may occur in this study should be reported directly to the Sponsor within 5 working days and to the EC, as required per EC guidelines. Participants experiencing Adverse Events must be treated by the treating physician per standard clinical practice at the institution.

The following information should be obtained for each AE:

1. **Event description.** Every effort must be made to report the underlying condition or unifying diagnosis for the event. To avoid vague, ambiguous or colloquial expressions, the AE should be recorded in standard medical terminology rather than the subject's own words when possible. Signs and symptoms that are considered unrelated to an encountered syndrome or disease should be recorded as individual AEs on the CRF (e.g., if congestive heart failure and severe headache are observed at the same time, each event should be recorded as an individual AE).

   In addition, AEs occurring secondary to other events (e.g., sequelae) should be identified by the primary cause (i.e., a "primary" AE, if clearly identifiable, generally represents the most accurate clinical term to record on AE CRF; events occurring secondary to the primary event should be described in the narrative description of the case.

2. **Duration:** The date of onset and date of resolution should be reported. Every effort should be made to capture the exact dates.

3. **Outcome:** The final status of the event should be reported as resolved, ongoing, or if it resulted in death. If the event is present at the final study visit, the ongoing box must be marked.

4. **Severity:** The severity of the event must be reported as mild, moderate, or severe using the following definitions:

- **Mild:** Aware of sign or symptom, but easily tolerated
- **Moderate:** Discomfort enough to cause interference with usual activity
- **Severe:** Incapacitating with inability to work or do usual activity

5. **Action taken**: Treatment of the event may be reported as none, medical and/or surgical.

6. **Seriousness:** Determined by using the criteria in Section 6.1.

7. **Relationship to device (study device or ancillary device) and/or procedure.** The relationship to device and study procedure will be assessed using the following criteria.
    - **Not related:** no temporal association or the cause of the event has been identified, or the device or procedure cannot be implicated.
    - **Possible:** temporal association, but other etiologies are likely to be the cause; however, the involvement of the device or procedure cannot be excluded.
    - **Probable**: the relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
    - **Causal:** temporal association; other etiologies are possible but unlikely.

    If any AE is considered to be "possibly related" or "related" to the use of the study device, that event will be classified as an ADE or a SADE. Any reported AEs will be assessed by the reporting investigator.

6.3 REPORTING/RECORDING OF AES

Throughout the course of the study, all efforts will be made by the investigator to remain alert to possible AEs. The first priority will be the safety of the subject and providing appropriate medical intervention. The period of observation for collection of AEs starts at index procedure until study completion.

6.4 ADVERSE EVENTS REPORTING

The Investigator must complete and submit the AE Case Report Form (CRF) containing all information required by local and/or regional regulations to the Sponsor and Clinical Research Organization (CRO) by fax or email immediately (within 24 hours of awareness).

Sponsor Contact:	Karl Firth
Telephone:	+45 31 32 47 45
Email:	KPF@cathvision.com

The AE CRF must be signed by a medically qualified investigator (as identified on the delegation of authority log). The signature confirms the accuracy and completeness of the SAE/SADE data as well as the investigator causality assessment including the explanation for the causality assessment.

In addition, the Investigator will report adverse events to the reviewing EC (as applicable) according to the local reporting requirements. Upon notification of SAEs, the Sponsor will initiate and complete a review and evaluation of the event within timeframes that will maintain reporting

compliance with applicable regulatory agencies. The Sponsor or designee will report all SAEs and device deficiencies that could have led to an SADE to the Competent Authority in accordance with EU Regulation 2017/745 and all applicable national regulations.

Investigators must submit safety reports as required by their EC within the required timelines. Documentation of the submission and receipt by the EC of should be retained by the study site.

In the event of a subject's death, the Investigator will make reasonable effort to obtain a copy of the autopsy report and/or death summary. The Investigator will determine the cause of death and its relationship to the investigational device; the Investigator will record results on the AE CRF. The Investigator will include copies of an autopsy report, if available, and/or a death summary with this form.

6.5 ANTICIPATED ADVERSE EVENTS

There are no anticipated Adverse Events specifically associated with the use of the CathVision ECGenius® system.

Arrythmias requiring an EP procedure that are chronic but stable, and present at screening, should not be recorded as an AE. Changes in a chronic condition or disease that are consistent with natural disease progression are NOT considered AEs and should not be recorded. These medical conditions should be adequately documented in the subject's cardiac history. However, medical conditions present at enrollment that worsen in intensity or frequency in a manner inconsistent with the natural course of the disease during the EP and/or ablation procedures and during the study should be reported and recorded as AEs.

A recurrence of an atrial tachyarrhythmia requiring hospitalization in order to administer cardioversion within the blanking period is within the scope of treatment for chronic but stable AF patients. This will not be considered an adverse event. Self-limiting pericarditis attributable to the ablation procedure, defined as pleuritic chest discomfort with or without pericardial rub and ECG changes, is not considered an adverse event.

The expected rates of occurrence of these anticipated AEs using the study device are expected to be the same as the rate experienced when using commercially available EP recording systems for the same indication. The mitigations and treatments for these AEs will follow published guidance for the same AEs occurring with other commercially available devices[1].

Anticipated AEs associated with arrhythmia and EP procedures include, but are not limited to:

- Air embolism
- Allergic reaction (including anaphylaxis)
- Anesthesia reaction
- Angina
- Aorto-right atrial fistula
- Arrhythmias, including exacerbation of pre-existing atrial fibrillation
- Arterial-venous fistula
- Cardiac perforation/ tamponade

- Cardiac thromboembolism
- Cardiac or respiratory arrest
- Catheter entrapment
- Cerebrovascular incident / Stroke
- Chest pain/discomfort
- Congestive heart failure
- Coronary artery dissection
- Coronary artery spasm
- Coronary artery thrombosis / occlusion
- Death
- Diaphragmatic paralysis
- Endocarditis
- Esophageal ulceration
- Gastroparesis
- Heart failure / pump failure
- Hemoptysis
- Hemothorax
- Hypotension
- Hospitalization (initial and prolonged)
- Increased creatinine phosphokinase (CPK) level
- Infections
- Laceration
- Leakage of air or blood into the lungs or other organs due to perforation
- Left atrial esophageal fistula
- Major bleeding, requiring surgery or transfusion
- Myocardial infarction
- Obstruction or perforation or damage to the vascular system
- Pericarditis
- Pericardial effusion
- Phrenic nerve damage including Diaphragmatic paralysis
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pulmonary edema
- Pulmonary embolism
- Pulmonary vein dissection
- Pulmonary vein thrombus
- Pulmonary hypertension
- Respiratory depression
- Skin burns
- Severe PV stenosis or complete occlusion, even asymptomatic
- Tamponade, potentially requiring surgery
- Temperature elevation or fever
- Transient Ischemic Attack (TIA)

- Thromboembolism
- Thrombosis
- Unintended complete or incomplete AV, Sinus node, or other heart block or damage
- Valve damage
- Vascular bleeding / local hematomas / ecchymosis
- Vasovagal reactions
- Ventricular tachyarrhythmia
- Volume overload

6.6 DEVICE DEFICIENCIES

Device deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance.

Note, device deficiencies include malfunctions and use errors. All device deficiencies that occur during the study will be recorded in the corresponding CRF.

Device malfunction: failure of an investigational medical device to perform per its intended purpose when used in accordance with the instructions for use.

User 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.

The Device Deficiency CRF is specific for reporting all device deficiencies that occur during the study, whether or not they were associated with an adverse event. Device Deficiency CRFs should be submitted to the Sponsor within 24 hours of the occurrence defining the device deficiency.

Anticipated device deficiencies and malfunctions from any standard of care EP system include, but are not limited to:

- Catheter deflection deficiency or failure
- Malfunction of a catheter electrode
- Malfunction of a catheter temperature sensor
- Unexpected termination of ablation due to internal system error
- Failure to initiate ablation due to internal system error
- Temporary or sustained loss of catheter navigation/visualization capability/signal

Record any CathVision ECGenius® system deficiencies and malfunctions, including but not limited to:

- ECGenius® system issues (Cube® EPAMP/RecSW)
    - Not able to power on
    - Power indicators not on
    - Not able to connect to the standard of care EP system
    - Note able to retrieve signal from standard of care EP system
    - Not able to power down
    - Database issues

    - Backup data issues
    - Not possible to clear fault without reboot
- ECGenius® Recorder Software
    - Malfunction
    - Loss of power
    - Loss of waveform
    - Recording issues (interruption, stop)
    - Not able to create patient
    - Not able to save patient
    - Live Mode issues (not able to create/resume patient, etc)
    - Review Mode issues (not able to retrieve a patient)
    - SW crashes
    - SW loses connection to EPAMP
    - Limitation: Only possible to review the latest recording file, while streaming is active
    - Bug: Not possible to use the notch filter, if high-pass and low-pass is set to 'None'
- Host Computer Malfunctions
    - Not able to boot/start
- User errors
    - Not recording data

7. STATISTICAL METHODS

7.1 SAMPLE SIZE CALCULATION

This prospective, single center, feasibility study is intended to collect data from patients in AF rhythm in order to test the feasibility of displaying changes in signal complexity. As a result, no formal statistical hypothesis was applied to derive the sample size. The selection of the sample size was made using a non-probability, purposive method.

If subjects receive treatment without meeting all the CIP-required conditions, they are counted in the Intent-to-Treat (ITT) population, they will not be deregistered from the clinical investigation, and they should complete all follow-up requirements. These subjects are considered CIP deviations, and are excluded from the sample size calculation and endpoint analysis. For a detailed description of the statistical analysis with respect to the enrolled population and deviations, refer to the Statistical Analysis Plan (SAP).

7.2 DESCRIPTIVE ANALYSES

Continuous variables will be summarized using standard quantitative statistics: number of available observations, mean, standard deviation, median, quartiles, and range (minimum and maximum observed values). The number of missing observations, if any, will also be summarized.

Categorical variables will be summarized using classical frequency statistics: number of non-missing observations and percentages by categories. Number and percent of missing data, if any, will also be summarized.

There are no predefined criteria for terminating the study based on statistical outcomes. Missing data will not be replaced or imputed.

Additional statistical considerations are detailed in the Statistical Analysis Plan (SAP).

8. STUDY CONDUCT

8.1 STUDY COMPLIANCE

This Study will be conducted in compliance with the CIP, the signed Clinical Study Agreement and with the ethical principles stated in the latest version of the Declaration of Helsinki (2013), the applicable guidelines for good clinical practices, EU MDR 2017/745, EN ISO 14155:2020 (Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice), and the applicable local and international regulations, in order to provide the greatest protection of the individual. Any deviations from the CIP that may affect the safety and welfare of study participants will be immediately reported to the Sponsor and to the Ethics Committee (EC) per each institution's guidelines.

8.2 ETHICS COMMITTEE (EC) AND COMPETENT AUTHORITY (CA)

The Study will not start without the written approval of the EC and the Competent Authority. Upon Study termination, if applicable, the Competent Authorities and ECs will be notified.

By signing the Clinical Study Agreement, the investigator is assuring that an EC will be responsible for the initial and continuing review of the proposed Study. A copy of the EC approval letter for the CIP, the informed consent, and the CIP signature page must be submitted to the Sponsor or its Designee prior to release of investigational supplies to the study site. The approval letter must refer to the specific CIP and the informed consent form. Any Investigator who is also a member of the EC is not to participate in the study approval decision. This non-participation must be noted in the approval letter. The study site must maintain an accurate and complete record of all reports, documents and other submissions made to the EC concerning this CIP.

Any report of withdrawal of EC approval will be submitted to the Sponsor or its Designee within five (5) working days.

The Sponsor or its Designee is responsible for obtaining regulatory approval for the Study from the Competent Authority. No subjects may be enrolled in the Study until written notification of such approval has been given by the Sponsor. The Sponsor or its Designee is responsible for reporting SAE and Device Deficiencies that might have led to a SADE as appropriate to the relevant Competent Authority. The Sponsor or its Designee is responsible to provide the relevant Competent Authority with the study final report within 12 months of the study termination.

8.3 INFORMED CONSENT PROCESS

It is the responsibility of the Investigator to inform each subject prior to the screening evaluation, of the purpose of this Study, including possible risks and benefits and document the informed consent process in the subject's chart. Any changes made to the informed consent must be approved by the Sponsor or its Designee, prior to submission to an EC. After approval by the Sponsor or its

Designee, the informed consent must be submitted to and approved by the applicable EC.
The process of obtaining informed consent at a minimum shall include the following steps:

- Ensure that the principal investigator or its authorized Designee conducts the informed consent process
- Include all aspects of the clinical investigation that are relevant to the subject's decision to participate throughout the clinical investigation
- Avoid any coercion or undue improper influence on, or inducement of, the subject to participate
- Not waive or appear to waive the subject's legal rights
- Use native non-technical language that is understandable to the subject
- Provide ample time for the subject to read and understand the informed consent form and to consider participation in the clinical investigation
- Include personally dated signatures of the subject and the principal investigator or an authorized Designee responsible for conducting the informed consent process
- Provide the subject with a copy of the signed and dated informed consent form and any other written information
- Ensure important new information is provided to new and existing subjects throughout the clinical investigation

One original informed consent form is to be retained by the study site and a copy is to be given to the subject. The informed consent process must be documented in the subject's source/medical record.

The informed consent must be written in a language in which the subject is fluent. If a foreign language translation is required, a statement of certification of the translation must be issued. Regulations require that foreign language informed consent forms be submitted to the EC for approval. The investigator must forward a copy of the consent form, the certified foreign language translation and an EC approval letter to the Sponsor or its Designee.

8.4 PROTOCOL DEVIATIONS

The Investigator is not allowed to deviate from the protocol.

Under emergency circumstances, deviations from the Clinical Study Protocol to protect the rights, safety, and well-being of human subjects may proceed without prior approval of the Sponsor and the EC. These deviations will be reported to the Sponsor and the EC as soon as possible after detection, but no later than 24-hours from the time of the deviation, as required.

Deviations must be documented on the appropriate Protocol Deviation CRF. If a Clinical Monitor becomes aware that an Investigator is not complying with the signed Investigator's Agreement, the Clinical Study Protocol, the requirements of GCP/ICH Guidelines or other applicable regulations, or any conditions of approval imposed by the reviewing EC, the Sponsor or designee will immediately either secure compliance or terminate the Investigator's participation in the investigation. The Investigator will be required to return all investigational components of the study device and system unless this action would jeopardize the rights, safety, or welfare of a patient.

Protocol deviations will be analyzed by the Sponsor for the impact to the overall integrity of the study. Disqualification is warranted when an Investigator has repeatedly or deliberately violated governing regulations or has repeatedly or deliberately submitted false information in any report. Where protocol deviations occur, which do not warrant disqualification from a study, the Sponsor or designee will implement appropriate corrective and preventive actions, including repeat training as deemed necessary.

8.5 STUDY TRAINING

The study device is intended for use by experienced medical personnel. The Investigator and study staff will receive Sponsor-led training on the proper use of the device to ensure the study team is familiar with its use prior to study enrollment and participation.
The study center will undergo a study initiation visit including but not limited to a review of the following:

- Study Protocol
- Study Procedures and Assessments
- Process for obtaining Informed Consent and completing Informed Consent Form
- Reporting requirements
- electronic Case Report Form (eCRF) completion and Good Documentation Practices
- Study device overview, usage, and accountability
- Protection of patient confidentiality
- Good Clinical Practices

8.6 STUDY MONITORING AND SOURCE DOCUMENTATION

The Sponsor or its designee will meet with investigators prior to the initiation of the study at their site to review the adequacy of the subject population, facilities, equipment for the needs of the study, and to familiarize the investigator with the study protocol and the investigational device.

CathVision or designee will monitor the investigational site to ensure that the study is conducted in accordance with the protocol, the Declaration of Helsinki (2013), the applicable guidelines for good clinical practices, EU MDR 2017/745, EN ISO 14155:2020 (Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice), and the applicable local and international regulations.

During monitoring visits, the monitor will review the source documents used for completion of the CRFs to verify the accuracy and completeness of the information contained in those reports in preparation for retrieval. CRFs must be completed within three to five working days of the subject visit. Source documents must contain all data entered in the CRFs. Source documents may include a subject's medical record, hospital charts, clinic charts, the Investigator's study files, the results of diagnostic tests such as laboratory tests, EKGs, 24-hour Holter monitoring, and the like. All data generated during this study and the source documents from which they originated are subject to inspection by the Sponsor or its representatives and/or regulatory agencies.

CathVision intends to monitor the investigational site at an interval consistent with the screening rate. At least 2 monitoring visits will be scheduled (based on enrollment), after approximately 10 subjects have been enrolled at the site.

To maintain subject safety, data quality and integrity, during unexpected circumstances (i.e., COVID-19), alternative approaches to on-site visits, such as; central monitoring, telephone contact with the site(s) to review study procedures, study participant status, and study progress; or remote monitoring of individual enrolled subjects may occur.

As required by the ISO 14155:2020, the conduct and monitoring of the clinical investigation will be conducted in accordance with the Sponsor's approved monitoring plan.

8.7 STUDY CLOSE-OUT

Upon completion of the study, the clinical monitor will conduct a final visit (close-out) at the site. At the time of the site close-out visit, the Monitor will collect all outstanding study documents, ensure that the Investigator's files are accurate and complete, review record retention requirements with the Investigator, make a final accounting of all study supplies, and ensure that all applicable requirements are met for the study. The observations and actions made at this visit will be documented in a final close-out report.

8.8 PROTOCOL AMENDMENTS

The Sponsor will document modifications to the protocol in the form of a written amendment. All protocol modifications must be approved by the EC before implementation. In the case of a medical emergency, to remove immediate apparent hazard to subjects, a change may be made preferably after discussion with the Sponsor or its designee. In these instances, the EC will be notified as soon as possible.

8.9 STUDY INSURANCE

In order to cover possible damage to health in relation to participation in this Study, the Sponsor has obtained appropriate insurance coverage. The insurance certificate and policy can be made available by the Sponsor upon request.

9. DATA HANDLING

The Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical investigation. CRF data collection will be performed through a secure web portal and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

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

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

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress

records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the EC and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical investigation.

For a detailed description of procedures used for data entry and collection, data review and data cleaning, and issuing, resolving data discrepancies and methods for data base lock. please refer to the Data Management Plan (DMP). The DMP will include procedures for the verification, validation and securing of electronic clinical system, if applicable, as well as procedures for maintaining and protecting subjects privacy. If appropriate, the DMP may be updated throughout the duration of the clinical investigation. All revisions will be tracked and document controlled.

9.1 CONFIDENTIALITY

In accordance with GDPR and the national data protection laws, all information concerning the subjects in the study must be treated as strictly confidential by all persons involved in the study. Health data will be recorded and forwarded to the Sponsor or its designee, and participating EC, for evaluation as required. Any information that is obtained in connection with this study that can be identified with the subjects will remain confidential. Any data that may be published in scientific journals will not reveal the identity of the study participants

The investigator acknowledges that all information acquired from the Sponsor or its designee or developed or acquired in connection with the study are strictly confidential. The investigator will not disclose any confidential information to any third party nor use confidential information for any purpose without first obtaining the consent of the Sponsor in writing. Such consent shall be deemed to have been given for disclosure to any person for whom the investigator is responsible at their center, but only so far as required for the study, and, in the case of disclosures to staff, only if such staff are bound by obligations of confidentiality no less strict than those set out herein.

9.2 RECORD KEEPING AND RETENTION

Data generated for the study should be stored in a limited-access file area and be accessible only to representatives of the study site, the Sponsor and its representatives, and relevant health authorities/regulatory agencies. All reports and communications relating to study subjects will identify subjects only by initials and subject identification number. Complete subject identification will be kept by the investigator. This information will be treated with strict adherence to professional standards of confidentiality.

All study-related records must be maintained for at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. The Sponsor will notify the Investigator when records are no longer needed. The Investigator will not discard any records without notifying the Sponsor. If the Investigator moves from the current investigational site, the Sponsor should be notified of the name of the person who will assume responsibility for maintenance of the records at the investigational site or the new address at which the records will be stored. The Investigator will notify the Sponsor as soon as possible in the event of accidental loss or destruction of any study documentation.

9.3 INVESTIGATOR FINAL REPORT

The investigator shall provide the EC and the Sponsor with an accurate final report within 2 months of completion, termination, or discontinuation of the study. The final report may not precede final data submission which has not been monitored.

9.4 STUDY REPORT AND PUBLICATION

The results of the study may be submitted for publication. Upon the prior written consent of the Sponsor, the Investigator shall have the rights to publish papers related to the Study.

If written permission from the Sponsor is provided, the PI may publish and/or present the results of the study conducted at their site, provided that, prior to any such publication or presentation, the site and/or the PI shall provide the Sponsor with two (2) hard copies and one electronic copy of any materials intended for publication or presentation at least sixty (60) days prior to the submission of manuscripts. The Sponsor shall then have sixty (60) days from the receipt of such materials to review and provide the site and/or the PI with written comments.

10. RESPONSIBILITIES

10.1 INVESTIGATOR RESPONSIBILITIES

The Principal Investigator of an investigational site is responsible for ensuring that the Study is conducted in accordance with the Clinical Study Agreements, the CIP, ISO 14155:2020, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing EC, and prevailing local and/or country laws and/or regulations, whichever affords the greater protection to the subject. In addition, the Investigators are responsible for:

- Ensuring that the Study is conducted with the express approval of the CA/EC
- Ensuring that conducting the Study will not give rise to conflicts of interest
- Ensuring that informed consent is obtained appropriately and that the conditions of informed consent are complied with
- Ensuring that all subjects entering the Study conform to the Clinical Investigation Plan
- Ensuring compliance with the CIP
- Ensuring the appropriate completion of all CRFs
- Maintaining all records as described in the CIP and according to the national guidelines and laws and the institution's requirements
- Ensuring the documentation, maintenance and correctness of the device accountability
- Ensuring that all investigational study material are returned to the Sponsor at the end of Study
- Informing the Sponsor of all adverse events and adverse device effects in a timely manner and informing the EC of any serious adverse device effects as applicable
- Informing the Sponsor in writing of the reason(s) for any withdrawal of any CA/EC approval

• Ceasing the enrolment of subjects immediately in the event of the withdrawal of any CA/EC approval

10.2 SPONSOR RESPONSIBILITIES

All information and data sent to the Sponsor concerning subjects or their participation in this Study will be considered confidential. Only authorized Sponsor or Sponsor's Designee will have access to these confidential records. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this Study. Study data collected during this Study may be used by the Sponsor for the purposes of this Study, publication, and to support future research and/or other business purposes. All data used in the analysis and reporting of this Study will be without identifiable reference to specific subject name and will be pseudonymized. The Sponsor or authorized Designees of the Sponsor may be present at the EP procedures to provide technical and study specific assistance and shall assist with the collection of recorded technical data via the use of Technical Source Forms. The CathVision ECGenius® System is password protected and only the Sponsor is allowed to work with the study device. Any data collected by the Sponsor's Designee will be verified and counter signed by the Investigator. The Sponsor's Designee will not:

• Practice medicine

• Provide medical diagnosis or treatment to subjects

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