Utilizing Novel Dipole Density Capabilities to Objectively Visualize the Etiology of Recurrent Atrial Fibrillation Following a Failed AF Ablation

(RECOVER AF)

Protocol: CLP-AF-004, Revision 02

07 June 2018

Sponsor:

Acutus Medical, Inc.

2210 Faraday Ave, Suite 100

Carlsbad, CA 92008

CONFIDENTIALITY STATEMENT

PROTOCOL SIGNATURE PAGE

CLP-AF-004 Rev 02

The signature below constitutes the approval of this Clinical Investigational Plan (CIP) and provides assurances that this clinical study will be conducted in accordance with all stipulations of the CIP including all statements regarding patient confidentiality. The CIP will be followed according to all national and local legal and regulatory requirements.

Site Investigator Printed Name

Site Investigator Signature

Date

dd-mmm-yyyy

Revision History

Revision #	***Date***	***Description***
01	30 October 2017	Initial release
02	07 June 2018	Changed inclusion criteria, modified Schedule of Events to include retreatment procedure and the application of an additional continuous ECG monitor, changed contact information, and added Medical Monitor.

1 CLINICAL STUDY SYNOPSIS

STUDY TITLE	Utilizing Novel Dipole Density Capabilities to Objectively Visualize the Etiology of Recurrent Atrial Fibrillation Following a Failed AF Ablation (RECOVER AF)
DEVICE NAME	AcQMap® High Resolution Imaging and Mapping System
DEVICE SHORT NAME	AcQMap
DEVICE COMPONENTS	The AcQMap System consists of the following components: • The AcQMap 3D Imaging and Mapping Catheter (AcQMap Catheter) • The AcQGuide® Steerable Delivery Sheath • The AcQMap Console • The AcQMap Workstation • The AcQMap Patient Electrode Kit
INDICATION FOR USE **(INTENDED USE)**	The AcQMap Imaging and Mapping System is intended to be used in the right and/or left atria to visualize the selected chamber and display atrial electrical impulses.
SPONSOR	Acutus Medical®, Inc. 2210 Faraday Ave., Suite 100 Carlsbad, CA 92008
STUDY OBJECTIVES	To evaluate the performance and efficiency of the AcQMap Imaging and Mapping System in an ablation retreatment procedure for recurrent atrial fibrillation following a failed AF ablation
STUDY DESIGN	A prospective, single-arm, multi-center, multi-national, non-randomized, post-market study designed to provide clinical data regarding the use of the AcQMap High Resolution Imaging and Mapping System during an atrial fibrillation retreatment ablation procedure. The patient population includes men and women, eighteen (18) years of age or older, who in the past twenty-four (24) months have had no more than two (2) previous left-atrial ablations for AF treatment. The treatment plan must include evaluation and ablation (as indicated) of pulmonary vein reconnections plus AcQMap guided non-PV substrate ablation. Subject assessments will occur at screening, procedure, hospital discharge, 3-, 6-, and 12-months.
SAMPLE SIZE	Enrollment of up to one hundred (100) subjects that complete the ablation procedure using the AcQMap System
CLINICAL SITES	Up to fifteen (15) Clinical Sites
DURATION	Enrollment is anticipated to take approximately twelve (12) months. Post-procedure assessments will occur at 3-, 6-, and 12-months. The

	total study duration is anticipated to be approximately twenty-four (24) months.
OUTCOME MEASURES	The measurable objectives are a descriptive analysis of the following: • At the procedure conclusion, confirmation of electrical isolation of all pulmonary veins and elimination/modification of all non-PV targets as identified by the AcQMap System • Recording of all subjects who are atrial fibrillation free from events lasting > 30 seconds at 6-, and 12-months as measured by a 48-hour continuous ECG o A subset analysis of AAD use o A subset analysis of subjects with freedom from AF/AT/AFL events lasting > 30 seconds as measured by a 48-hour continuous ECG • Documentation of procedure data including total time, fluoroscopy time, ablation times for PVI, and ablation times for non-PV targets • Safety – Recording of all device and procedure related safety events through 24 hours post-ablation
INCLUSION CRITERIA	The patient population will consist of men and women eighteen (18) years of age or older, scheduled for a repeat endocardial ablation of AF following a failed ablation for atrial fibrillation. A potential subject will be eligible for study enrollment only if all the following inclusion and none of the exclusion criteria apply: IC 1 Male or female eighteen (18) years of age or older IC 2 Currently scheduled for a repeat endocardial ablation of AF IC 3 Willingness, ability, and commitment to participate in baseline and follow-up evaluations for the full length of the study IC 4 Willingness and ability to give informed consent
EXCLUSION CRITERIA	EC 1 In the opinion of the Investigator, any known contraindication to a left-atrial ablation or concerns for left-atrial thrombus EC 2 No more than two (2) previous left-atrial ablations EC 3 Atrial arrhythmias secondary to electrolyte imbalance, thyroid disease, or any other reversible or non-cardiac cause EC 4 Structural heart disease or implanted devices as described below: a. An implanted pacemaker or ICD b. Previous cardiac surgery, ventriculotomy, or atriotomy (excluding atriotomy for CABG) c. Previous cardiac valvular surgical or percutaneous procedure, or prosthetic valve d. Interatrial baffle, closure device, patch, or PFO occluder e. Presence of a left atrial appendage occlusion device f. Unstable angina or ongoing myocardial ischemia

	EC 5 History of blood clotting or bleeding disease EC 6 Pregnant or lactating (current or anticipated during study follow up) EC 7 Current enrollment in any study protocol sponsored by Acutus Medical or any other study that may impact the results of RECOVER AF EC 8 Any other condition that, in the judgment of the investigator, makes the patient a poor candidate for this procedure, the study, or compliance with the protocol (includes vulnerable patient population, mental illness, addictive disease, terminal illness with a life expectancy of less than two years, extensive travel away from the research center, etc.)
DATA COLLECTION	• Screening data to include demographics, arrhythmia history, current AAD use, and previous AF ablation history (3D system use, ablation targets including PV and non-PV locations, etc.). • Procedure data to include procedure time, fluoroscopy time, maps of ablation targets, pre-and post-procedure rhythm, DCCV for conversion, and a post-ablation AcQMap in the procedure ending rhythm. All alterations to ablation due to esophageal proximity will be noted. • Follow-up data to include safety events reported through discharge, continuous ECG monitor (≥ 48-hr), and AAD medications at 3-, 6- and 12-months post-procedure.
STATISTICAL METHODS AND ANALYSIS SUMMARY	Descriptive statistical analysis of all data recorded
FOLLOW-UP EVALUATIONS	See Table Below

Table 1: Schedule of Events

	Screening & Baseline	Procedure	Discharge	3-month (± 14 days)	6-month (± 30 days)	12-Month (± 30 days)	Retreatment Visit (if medically necessary)
CIP Informed Consent	X						
Medical History	X						
Arrhythmia Management Assessment				X	X	X	X
Cardiovascular Exam	X		X				X
AAD Medications	X	X	X	X	X	X	X
Procedure Data		X					X
Adverse Events		X	X				X
12-lead ECG		X	X	X	X	X	X
Continuous 48-hr ECG monitor				X	X	X	X (prior to retreatment)

2 TABLE OF CONTENTS

3 CONTACT INFORMATION

3.1 Name and Address of Sponsor

Acutus Medical, Inc.

2210 Faraday Ave., Suite 100

Carlsbad, CA 92008

4 ABBREVIATIONS

3D	Three Dimensional
AAD	Anti-Arrhythmic Drug
ACT	Activated Clotting Time
ADE	Adverse Device Effect
AE	Adverse Event
AF	Atrial Fibrillation
AFL	Atrial Flutter
AIU/PIU	Ablation Interface Unit/Patient Interface Unit
AT	Atrial Tachycardia
ATP	Adenosine
CABG	Coronary Artery Bypass Grafting
CIP	Clinical Investigational Plan
CMP	Clinical Monitoring Plan
CPM	Clinical Project Manager
CRA	Clinical (or Contract) Research Associate
CRO	Contract Research Organization
CRF	Case Report Form
CTI	Cavo-tricuspid Isthmus
DCCV	Direct Current Cardioversion
DMP	Data Management Plan
EC	Ethics Committee
eCRF	Electronic Case Report Form
ECG	Electrocardiogram
EDC	Electronic Data Capture
EGM	Electrogram
FDA	Food and Drug Administration
GCP	Good Clinical Practices
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IA	Investigator Agreement
ICD	Implantable Cardioverter Defibrillator
IFU	Instructions For Use
ISF	Investigator Site Files
ISO	International Organization for Standardization
IV	Intravenous
LA	Left Atrium
LFU	Lost to Follow-Up
OM	Operator's Manual

PAF	Paroxysmal Atrial Fibrillation
PFO	Patent Foramen Ovale
PI	Principal Investigator
PV	Pulmonary Vein
PVI	Pulmonary Vein Isolation
QAP	Quality Assurance Procedure
RF	Radio Frequency
RMV	Routine Monitoring Visit
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SIV	Site Initiation Visit
SOC	Standard of Care
SOP	Standard Operating Procedure
SVT	Supraventricular Tachycardia
SQV	Site Qualification Visit
TIA	Transient Ischemic Attack
TMF	Trial Master File
TS	Transseptal Puncture
UADE	Unanticipated Adverse Device Effect
USFDA	United States Food and Drug Administration
WACA	Wide Area Circumferential Ablation

5 INTRODUCTION TO THE CLINICAL INVESTIGATIONAL PLAN/PROTOCOL

5.1 Background

Atrial fibrillation (AF) is among the most prevalent arrhythmias in the world today affecting approximately 1.5-2% of the general population. The age of patients with AF is steadily rising and now averages between 75 and 85 years of age. AF is associated with a five-fold risk of stroke, a three-fold incidence of congestive heart failure, and higher mortality.[1]

Symptoms arise from the rapid, irregular rhythm as well as the loss of cardiac pump function related to uncoordinated atrial contractions. These uncoordinated contractions also allow blood to pool in the atria and may ultimately lead to thromboembolism and stroke.

AF is characterized by a chaotic contraction of the atrium in which an electrocardiogram (ECG) recording is necessary to diagnose the arrhythmia. Any arrhythmia that has the ECG characteristics of AF and lasts sufficiently long for a 12-lead ECG to be recorded, or at least 30 seconds on a rhythm strip, should be considered an AF episode.[2,3]

The diagnosis requires an ECG or rhythm strip demonstrating: (1) Irregular RR intervals (in the absence of complete AV block), (2) no distinct P waves on the surface ECG, and (3) an atrial cycle length (when visible) that is usually variable and less than 200 milliseconds.[3]

AF can be characterized into four classifications:

- Paroxysmal AF (PAF) is defined as AF that terminates spontaneously or with intervention within seven days of onset.

[1] Camm AJ, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation--developed with the special contribution of the European Heart Rhythm Association. *Europace*, 2012 Oct; 14(10):1385-413

[2] Calkins H, Brugada J, Packer DL et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm*. Jun 2007;4(6):816–861

[3] Camm AJ, Kirchhof P, Lip GY et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J.* Oct 2010;31(19):2369–2429

- Persistent AF is defined as continuous AF that is sustained beyond seven days. It is further sub-stratified into early persistent AF (continuous AF > 7-days but ≤ 3 months).
- Long-standing persistent AF is defined as continuous AF of greater than 12 months duration.
- Permanent AF is defined as AF in which the presence of the AF is accepted by the patient (and physician). Within the context of any rhythm control strategy, including catheter ablation, the term permanent AF is not meaningful. The term permanent AF represents a joint decision by the patient and a physician to cease further attempts to restore and/or maintain sinus rhythm at a particular point in time.[4]

For many years, three major schools of thought competed to explain the mechanism(s) of AF: multiple random propagating wavelets, focal electrical discharges, and localized reentrant activity with fibrillatory conduction.[5,6,7,8,9] Significant progress has been made in defining the mechanisms of initiation and perpetuation of AF. One of the most important breakthroughs was the recognition that, in a subset of patients, AF was triggered by a rapidly firing focus and could be "cured" with a localized catheter ablation procedure.[10,11] This landmark observation caused the electrophysiology (EP) community to refocus its attention on the pulmonary veins (PVs) and the posterior wall of the left atrium (LA), as well as the autonomic innervation in that region. It also reinforced the concept that the development of AF requires a "trigger" and an anatomic or functional substrate capable of both initiation and perpetuation of AF.

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[4] Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS?APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation. Epub Heart Rhythm, May 12, 2017.

[5] Jalife J, Berenfeld O, Mansour M. Mother rotors and fibrillatory conduction: a mechanism of atrial fibrillation. *Cardiovasc Res*. May 2002;54(2):204–216.

[6] Nattel S. New ideas about atrial fibrillation 50 years on. *Nature*. Jan 10 2002; 415(6868):219–226.

[7] Dobrev D, Voigt N,Wehrens XH. The ryanodine receptor channel as a molecular motif in atrial fibrillation: pathophysiological and therapeutic implications. *Cardiovasc Res*. Mar 1 2011;89(4):734–743.

[8] Schotten U, Verheule S, Kirchhof P, Goette A. Pathophysiological mechanisms of atrial fibrillation: a translational appraisal. *Physiol Rev*. Jan 2011;91(1):265–325.

[9] Wakili R, Voigt N, Kaab S, Dobrev D, Nattel S. Recent advances in the molecular pathophysiology of atrial fibrillation. *J Clinical Invest*. Aug 1 2011;121(8):2955–2968

[10] Jais P, Haissaguerre M, Shah DC et al. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation*. Feb 4 1997;95(3):572–576.

[11] Haissaguerre M, Jais P, Shah DC et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med*. Sep 3 1998; 339(10):659–666.

Sustained high rates in the atrium and/or the presence of heart disease are associated with structural and electrophysiological remodeling of the atria and can alter the substrate even further and help to perpetuate AF.[12] AF can also be the result of preexisting atrial disease. Although much has been learned about the mechanisms of AF, they are not completely understood. Because of this, in the great majority of AF patients, it is not yet possible to precisely tailor an ablation strategy to a particular AF mechanism.

3D Mapping

Three-dimensional (3D) electroanatomical contact and non-contact mapping systems have been reported to facilitate ablation of AF by identifying anatomical structures and highlighting the location of ablated sites. This can guide the initial ablation and help identify existing gaps in an incomplete lesion set.[13] Additionally, electromagnetic navigation systems have been shown to substantially reduce the fluoroscopy time required for AF ablation.[14,15,16]

The AcQMap System

The AcQMap High Resolution Imaging and Mapping System (AcQMap System) has been designed to provide information on cardiac dipole densities as a function of time and project that information on an image of a cardiac chamber. In this study, the AcQMap System will collect data from the AcQMap 3D Imaging and Mapping Catheter (AcQMap Catheter) to create anatomical reconstructions of the chamber(s) being mapped and to create dipole density maps on those reconstructions. These maps will then be used to identify mechanisms of AF, which can be targeted for ablation.

[12] Everett TH 4th, Wilson EE, Verheule S, Guerra JM, Foreman S, Olgin JE. Structural atrial remodeling alters the substrate and spatiotemporal organization of atrial fibrillation: a comparison in canine models of structural and electrical atrial remodeling. Am J Physiol Heart Circ Physiol. Dec 2006;291(6):H2911–2923

[13] Hindricks G, Willems S, Kautzner J, De Chillou C, Wiedemann M, Schepel S, Piorkowski C, Risius T, Kottkamp H; EuroFlutter Investigators. Effect of electroanatomically guided versus conventional catheter ablation of typical atrial flutter on the fluoroscopy time and resource use: a prospective randomized. J Cardiovasc Electrophysiol. 2009 Jul;20(7):734-40.

[14] Sporton SC, Earley MJ, Nathan AW, Schilling RJ. Electroanatomic versus fluoroscopic mapping for catheter ablation procedures: a prospective randomized study. J Cardiovasc Electrophysiol. 2004 Mar;15(3):310-5.

[15] Kottkamp H, Hügl B, Krauss B, Wetzel U, Fleck A, Schuler G, Hindricks G. Electromagnetic versus fluoroscopic mapping of the inferior isthmus for ablation of typical atrial flutter: A prospective randomized study. Circulation. 2000 Oct 24;102(17):2082-6.

[16] Smeets JL, Ben-Haim SA, Rodriguez LM, Timmermans C, Wellens HJ. New method for nonfluoroscopic endocardial mapping in humans: accuracy assessment and first clinical results. Circulation. 1998 Jun 23;97(24):2426-32.

5.2 Clinical Study Design Justification

Previous clinical studies utilizing the AcQMap System in an ablation procedure for supraventricular tachycardias (SVTs) have initially demonstrated an acceptable safety profile when mapping and imaging cardiac chambers. The RECOVER AF study is a prospective, single-arm, multi-center, multi-national, non-randomized, post-market study designed to provide clinical data regarding the use of the AcQMap High Resolution Imaging and Mapping System during an atrial fibrillation retreatment ablation procedure. Recording of all Serious Adverse Events/Device Effects occurring during the first twenty-four (24) hours post-procedure will be used to assess the safety related to the AcQMap Catheter, AcQGuide Steerable Sheath, and the AcQMap System.

Since it is hypothesized the technology advances of dipole density mapping may better identify and more precisely direct lesion locations during atrial arrhythmia ablations, the study is additionally designed to record longer term (6- and 12-month) data on the effectiveness of the ablation procedure in the treatment of the arrhythmia. An analysis of treatment success (defined as freedom from atrial arrhythmias at 6- and 12-months), compared to literature based historical controls, may offer insight regarding the ability of the AcQMap System to effectively and accurately identify appropriate ablation targets.

Automatic, instantaneous, and simultaneous 3D display of the LA surface with associated charge densities may potentially shorten atrial arrhythmia ablation procedure time and provide an intuitive tool to rapidly identify and guide effective treatment.

5.3 Indication for Use Statement

The AcQMap Imaging and Mapping System is intended to be used in the right and/or left atria to visualize the selected chamber and display atrial electrical impulses.

5.4 Device Description

5.4.1 General System Description

The AcQMap System is designed to create a 3D image of a heart chamber's endocardial surface in which catheters can be navigated and a chamber-wide electrical activation map can be overlaid for percutaneous procedures. The AcQMap System should only be used by physicians thoroughly trained in electrophysiology procedures and trained on the use of the AcQMap System.

AcQMap System Hardware

The AcQMap System hardware consists of the AcQMap Console, AcQMap Workstation and the AcQMap Ablation Interface Unit/Patient Interface Unit (AIU/PIU). The AcQMap Console contains all electronics for interfacing with patient-contacting devices such as the AcQMap Catheter and the Patient Electrode Kit.

5.4.2 The AcQMap 3D Imaging and Mapping Catheter

The AcQMap 3D Imaging and Mapping Catheter is a diagnostic, sterile, single-use device that has a polymeric catheter torque shaft, an integral handle and a flexible, metallic deployable/retractable array.

5.4.3 AcQGuide Steerable Sheath

The AcQGuide Steerable Sheath is a single-use, sterile, delivery sheath consisting of a deflectable shaft with a lumen, integral handle with steering mechanism, hemostasis valve and flush port. The sheath is compatible with other Acutus Medical catheter products. The sheath can be placed within the desired heart chamber thus allowing the AcQMap Catheter to be introduced, deployed, and directed within the chamber as needed.

6 CLINICAL STUDY

6.1 Clinical Study Objective

The objective of the clinical study is to evaluate the performance and efficiency of the AcQMap Imaging and Mapping System in an ablation retreatment procedure for recurrent atrial fibrillation following a failed AF ablation.

6.2 Clinical Study Design

The clinical study is a prospective, single-arm, multi-center, multi-national, non-randomized, post-market study designed to provide clinical data regarding the use of the AcQMap High Resolution Imaging and Mapping System during an AF retreatment ablation procedure. The patient population includes men and women, eighteen (18) years of age or older, who in the past twenty-four (24) months have had no more than two (2) previous LA ablations for AF treatment. Subject assessments will occur at screening, procedure, hospital discharge, 3-, 6-, and 12-months.

6.2.1 Measurable Objective

The measurable objectives are a descriptive analysis of the following:

- At the procedure conclusion, confirmation of electrical isolation of all pulmonary veins and elimination/modification of all non-PV targets as identified by the AcQMap System

- Recording of all subjects who are atrial fibrillation free from events lasting > 30 seconds at 6- and 12-months as measured by a 48-hour continuous ECG
    - A subset analysis of AAD use
    - A subset analysis of subjects with freedom from AF/AT/AFL events lasting > 30 seconds as measured by a 48-hour continuous ECG
- Documentation of procedure data including total time, fluoroscopy time, ablation times for PVI, and ablation times for non-PV targets
- Safety - Recording of all device and procedure related safety events through twenty-four (24) hours post-ablation

6.3 Clinical Study Duration

Enrollment is anticipated to take approximately twelve (12) months. Post-procedure assessments will occur at 3-, 6-, and 12-months. The total study duration is anticipated to be approximately twenty-four (24) months.

6.4 Clinical Study Sample Size and Clinical Sites

Up to one hundred (100) patients will be treated at up to fifteen (15) clinical sites in Europe. The sample size will include only those that complete an ablation procedure using the AcQMap technology (Treatment Subjects).

6.5 Clinical Study Enrollment Definitions

For the purposes of this clinical study, the following definitions regarding the status of a subject will apply:

Pre-Treatment Subject – Any subject who has signed an informed consent form, is deemed study eligible by meeting all of the inclusion and none of the exclusion criteria, and who has the venous access portion of the ablation procedure initiated. Pre-Treatment subjects that do not complete the AcQMap procedure will be followed for adverse events through hospital discharge. In addition to the discharge eCRF, a study completion eCRF will be completed. No follow-up beyond the hospital discharge will be required.

Treatment Subject – Any pre-treatment subject who completes the ablation procedure using the AcQMap System. A completed ablation procedure is defined as a procedure where the PVI was evaluated and additional non-PV targets were mapped and ablated using the AcQMap System. Treatment subjects should be followed for all study outcome measures for the full duration of the clinical study.

6.6 Clinical Study Population

The patient population will consist of men and women eighteen (18) years of age or older, scheduled for a repeat endocardial ablation of AF following a failed ablation for atrial fibrillation.

A potential study subject will be eligible for study enrollment only if all the following inclusion and none of the exclusion criteria apply:

6.6.1 Inclusion Criteria

IC 1 Male or female eighteen (18) years of age or older

IC 2 Currently scheduled for a repeat endocardial ablation of AF

IC 3 Willingness, ability, and commitment to participate in baseline and follow-up evaluations for the full length of the study

IC 4 Willing and able to give informed consent

6.6.2 Exclusion Criteria

EC 1 In the opinion of the Investigator, any known contraindications to a left-atrial ablation or concerns for left-atrial thrombus

EC 2 No more than two previous left-atrial ablations

EC 3 Atrial fibrillation secondary to electrolyte imbalance, thyroid disease, or any other reversible or non-cardiac cause

EC 4 Structural heart disease or implanted devices as described below:

a. An implanted pacemaker or ICD
b. Previous cardiac surgery, ventriculotomy, or atriotomy (excluding atriotomy for CABG)
c. Previous cardiac valvular surgical or percutaneous procedure, or prosthetic valve
d. Interatrial baffle, closure device, patch, or PFO occluder
e. Presence of a left atrial appendage occlusion device
f. Unstable angina or ongoing myocardial ischemia

EC 5 History of blood clotting or bleeding disease

EC 6 Pregnant or lactating (current or anticipated during study follow up)

EC 7 Current enrollment in any study protocol sponsored by Acutus Medical or any other study that may impact the results of RECOVER AF

EC 8 Any other condition that, in the judgment of the investigator, makes the patient a poor candidate for this procedure, the study,

or compliance with the protocol (includes vulnerable patient population, mental illness, addictive disease, terminal illness with a life expectancy of less than two years, extensive travel away from the research center, etc.)

6.7 Subject Withdrawal

Individual subjects may withdraw their consent to participate in the study at any time. Also, an Investigator may discontinue a subject's participation in the study at any time to protect the safety, rights, or welfare of the subject.

Subjects missing follow-up visits will not be considered lost to follow-up (LFU) until adequate attempts to contact the subject have been made.

7 CLINICAL STUDY TREATMENTS AND FOLLOW-UP VISITS

7.1 Informed Consent

It is the responsibility of the Investigator to give each subject full and adequate verbal and written information regarding all aspects of the study procedure, device, and associated risks. A signed informed consent form (ICF) must be obtained from the subject before any study procedures not considered standard of care (SOC) for an AF ablation are undertaken. The informed consent form must be signed by the subject and witnessed by the Investigator (or designee). The original signed consent is filed in the subject's study records with one copy placed in the subject's medical notes and one copy provided to the subject.

7.2 Subject Screening and Baseline

The following information should be acquired to verify eligibility in the clinical study:

- Subject demographics
- Medical history review including:
  - Procedural data of the previous AF ablation(s) including date(s), ablation strategy (PVI, PVI plus, etc.) and advanced mapping systems used, if any
  - Current AADs
  - Date of most recent direct current cardioversion (DCCV) with duration of sinus rhythm following the cardioversion
- Review of all inclusion/exclusion criteria to confirm subject eligibility
- Cardiovascular Exam

7.2.1 Mapping and Ablation

The objective of this clinical study is to evaluate the performance and efficiency of the AcQMap System when mapping and imaging the left and right atria during retreatment procedures for recurrent atrial fibrillation. Therefore, the utilization of devices for 3D anatomic reconstruction, navigation, and electrical mapping will be limited to the AcQMap System. Ablation energies for PVI may include RF, cryo, or laser. Ablation strategies to create pulmonary vein isolation is at the discretion of the investigator and may include antral ablations, wide area circumferential ablation (WACA), or "single shot" therapy. Radio frequency (RF) ablation catheters utilized during the procedure must be limited to those compatible with the AcQMap System. All PVI ablation strategies and catheter types shall be recorded on the procedure eCRF.

Refer to the Instructions for Use and Training Materials for a thorough description of the AcQMap preparation and delivery into the left atrium.

7.2.2 Procedure Data Collection

Collection of data generated during the procedure should include:

- Recording of 12-lead ECG at procedure start
- Recording of 12-lead ECG for predominant atrial arrhythmia(s)
- Recording of 12-lead ECG at procedure completion
- Total procedure time (from first venous access to last cardiac catheter removed)
- Total ablation time for PVI and non-PVI ablations
- Total fluoroscopy time for the ablation procedure
- Recording of all DCCV used during the procedure
- Recording of all IV cardiac medications infused during the procedure
- All alterations to ablation strategies due to esophageal proximity

7.3 Follow-Up Procedures

Screening, procedure, and follow-up visits are outlined in Table 2.

7.3.1 Hospital Discharge

Subjects should be monitored with telemetry prior to hospital discharge for the documentation of recurrence of any atrial arrhythmias. A recurrence prior to discharge **should not** be considered an adverse event unless it delays the discharge.

The following evaluations should be completed prior to discharge:

- Evaluation of femoral access sites
- AADs at discharge
- Evaluation and recording of adverse events
- 12-lead electrocardiogram

7.3.2 Visits at Three, Six and Twelve Months

The following evaluations will be performed during each clinic follow-up visit. Data will be recorded on the Follow-Up eCRFs.

- Arrhythmia recurrence/treatment since last visit
- AAD use and changes since last visit
- DCCV history since last visit
- 12-lead electrocardiogram
- 48-hour continuous monitor (may include Holter recording, BardyDx CAM or equivalent)

7.4 Recurrence of Atrial Fibrillation/Atrial Flutter/Atrial Tachycardia

Occurrences of symptomatic AF or other tachyarrhythmias during the first 90 days post-ablation (blanking period) may be transient in nature and not associated with the long-term effectiveness of the ablation treatment. However, prolonged AF should be treated as soon as possible to maintain SR during the remodeling period. Treatment should follow the Investigator's SOC for arrhythmia recurrence, which may include a DCCV and/or AAD administration. If the Investigator elects to repeat an ablation, a 48-hour continuous ECG monitor will be worn within two weeks and no later than 3 days prior to the procedure to document the presenting rhythm. The AcQMap System will be used during the procedure. Procedure and discharge data will be collected as part of RECOVER AF. There will be no adjustments to the scheduled follow-up periods and the study will be completed at 12-months post RECOVER AF index procedure.

Table 2: Schedule of Events

	Screening & Baseline	Procedure	Discharge	3-month (± 14 days)	6-month (± 30 days)	12-Month (± 30 days)	Retreatment Visit (if medically necessary)
CIP Informed Consent	X						
Medical History	X						
Arrhythmia Management Assessment				X	X	X	X
Cardiovascular Exam	X		X				X
AAD Medications	X	X	X	X	X	X	X
Procedure Data		X					X
Adverse Events		X	X				X
12-lead ECG		X	X	X	X	X	X
Continuous 48-hr ECG monitor				X	X	X	X (prior to retreatment)

8 STATISTICAL METHODS

Analysis of all data generated by the clinical study will be reported with descriptive statistics. There are no hypotheses established for the study therefore, the study sample size has not been established for power.

9 ADVERSE EVENTS

The safety outcome measure for this post-market study is a recording of all device and procedure related safety events through twenty-four (24)-hours post-ablation. Any event that occurs through twenty-four (24)-hours post-ablation is considered an AE and will be recorded on an Adverse Event eCRF. Any medical conditions, problems, signs, symptoms, or findings occurring prior to the AcQMap ablation procedure are to be considered as pre-existing conditions. The investigator has the responsibility of classifying any event as related to a component of the AcQMap System or the ablation procedure.

Serious Adverse Events (SAEs)

A Serious Adverse Event is any adverse event that:[17]

- 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 congenital anomaly or birth defect

Reports relating to the subject's subsequent medical course following an SAE must be submitted to the Sponsor until the event has subsided or, in the event of permanent impairment, until the event has stabilized, and the overall clinical outcome has been ascertained.

[17] EN ISO 14155:2011 section 3.37

Adverse Device Effects (ADEs)

Adverse Device Effects (ADEs) are a subset of AEs. The ADEs are only those AEs caused by, or related to the device, including any AE resulting from insufficiencies or inadequacies in the instructions for use, the System components, or any product malfunction, including any event that is a result of a user error or intentional misuse.

With any procedure or treatment, there are known possible risks and complications. A list of known or anticipated AEs for the AcQMap System is found in the CIP/protocol, Instructions for Use (IFU) and OM.

Unanticipated Adverse Device Effects (UADEs)

Investigators are required to submit a report to the Sponsor as soon as possible of any suspected Unanticipated Adverse Device Effect (UADE) occurring during an investigation, but no later than five (5) business days after the Investigator first learns of the effect.

When an Investigator suspects an event meets the definition for a UADE, then the event, date of onset, seriousness, severity, duration, treatment, outcome, and relationship to device will be recorded on the Adverse Event CRF. Additionally, reports must be provided to the reviewing Ethics Committee (EC) per national and local requirements.

The Sponsor/manufacturer must then conduct an evaluation of the suspected UADE and report the results of the findings to the Notified Body and to all reviewing ECs and participating Investigators within five (5) business days after first receiving notice of the effect. Thereafter, the Sponsor shall submit such additional reports concerning the effect as the Notified Body requests.

9.1 Adverse Event Reporting

The Investigator is responsible for reporting all procedure and device related AEs that occur within the first twenty-four (24) hours of the ablation procedure. Initial reporting will be with the Adverse Event eCRF; however, additional information may be required by the Sponsor or any regulatory authority. The Investigator should report any SAEs, SADEs, or UADEs to the Sponsor as soon as possible after becoming aware of the event, but no later than five (5) business days after receiving knowledge of the event occurrence. All SAEs, SADEs, and UADEs will be documented on the Adverse Event eCRF along with an explanation of any medical treatment administered. Documentation should include the time of onset, complete description of the event, severity, duration, actions taken, and outcome.

9.2 Event Relationship to the Device

The Investigator should provide information regarding the relationship of the event to the procedure and/or the AcQMap System or any of the components (AcQMap Catheter, AcQGuide Sheath, or Patient Electrode Kit). The device relationships are defined in the table below:

Table 3: AE Relationships

Not Related	The cause of the AE is known and is not related to any aspect of the mapping and imaging portion of the ablation procedure.
Possibly Related	There is a reasonable possibility that the event may be related to the mapping and imaging portion of the ablation procedure. The AE has a **timely relationship** to the study procedure(s); **however, it follows no known pattern of response** and an alternative cause seems more likely or there is significant uncertainty.
Probably Related	It is probable that the event is related to the mapping and imaging portion of the ablation procedure. The AE has a **timely relationship** to the study procedure(s) and **follows a known pattern of response**, but a potential alternative cause may be present.
Definitely Related	The event is definitely related to the mapping and imaging portion of the ablation procedure. A related event has a strong temporal relationship and an alternative cause is unlikely.

9.3 Death Notice

When a site becomes aware of a subject's death, it should be reported to the Sponsor. Notification should be made to the reviewing EC per local requirements.

9.4 Device Complaint and Malfunction

Each clinical procedure will be attended by Acutus Medical personnel responsible for the proper use of the technology. If a malfunction occurs, the Sponsor representative will report the findings to the Clinical and Product Complaints departments. Evaluations of all complaints will follow Acutus Medical QAPs for complaint handling.

9.5 Adverse Event Analysis

All procedure and device related adverse events will be evaluated by a clinical representative for Acutus Medical. Reporting to convening ECs will follow local regulatory requirements.

10 RISK: BENEFIT ANALYSIS

10.1 Risks

The following adverse events are associated with electrophysiology mapping and ablation procedures:

- Adult Respiratory Distress Syndrome
- Air embolism
- Anemia
- Anesthesia reaction
- Aorto-right atrial fistula
- Arrhythmias
- Arteriovenous (AV) fistula
- AV or SA node damage
- Atrial esophageal fistula
- Cardiac perforation/tamponade
- Cardiac thromboembolism
- Cerebral infarct (hemorrhagic or thromboembolic)
- Chest pain/discomfort
- Complete heart block (transient or permanent
- Congestive heart failure
- COPD exacerbation
- Coronary artery spasm/dissection
- Coronary artery thrombosis/occlusion
- Death
- Diaphragmatic paralysis
- Dislodgement of ICD/pacemaker leads
- Elevated cardiac enzymes
- Endocarditis
- Local hematomas/ecchymosis
- Major bleeding, requiring surgery or transfusion
- Myocardial infarction
- Obstruction, perforation or damage to the vascular system
- Pericardial effusion
- Pericarditis
- Phrenic nerve damage
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism
- Pulmonary hypertension
- Pulmonary vein dissection
- Pulmonary vein stenosis
- Pulmonary vein thrombosis
- Radiation injury
- Respiratory depression
- Seizure
- Skin burns
- ST segment elevation
- Temporary complete heart block

- Fever
- Fluid overload
- Heart failure/pump failure
- Hemothorax
- Infection/sepsis
- Thromboembolism
- Transient ischemic attack (TIA)
- Valvular damage/insufficiency
- Vasovagal reaction

10.2 Mitigation of Risks

Pre-clinical research and ongoing clinical studies have demonstrated that the system is safe for human use. All potential risks have been evaluated and mitigation strategies have been implemented to reduce potential risks to acceptable levels. Acutus Medical believes that the potential benefits of the system outweigh the potential risks.

11 DATA QUALITY ASSURANCE

Acutus Medical will oversee the data collection for this study in accordance with Good Clinical Practices (GCP), regulatory requirements, the Data Management Plan (DMP), and corporate QAPs. Data will be collected and stored in an Electronic Data Capture (EDC) system. Data will be reviewed for accuracy and completeness by Acutus Medical (or designees). Any discrepancies will be resolved with the Investigator or designees, as appropriate. In order to preserve data integrity and security of the data, access to the study in the EDC will be controlled by Acutus Medical and shall be limited to appropriately trained personnel with assigned log-on credentials.

11.1 Site Data Management

For the duration of the study, the Investigator and their designees will maintain complete and accurate documentation, including but not limited to medical records, study progress notes, laboratory reports, signed patient ICFs, correspondence with the reviewing EC, correspondence with Acutus Medical (or designees) and study monitors, AE reports, and information regarding subject discontinuation/withdrawal or completion of the study.

The Investigator/Institution will permit direct access to source data and documents in order to complete study-related monitoring, audits, EC reviews, event adjudication, and regulatory inspections that may be performed. The Investigator will obtain, as part of the ICF process, permission for authorized Sponsor employees, study monitors or regulatory authorities to review, in confidence, any records that identify subjects in this study.

11.2 Subject Identification

Subjects will be identified on all eCRFs and source documents by a unique, anonymized identification reference number, which will be issued once the ICF has been signed. An identification reference number may not be reused for any reason.

11.3 Screen Failure Subjects

Subjects who are screened for the study but are not enrolled for any reason will not be followed and their data will not be used for any outcomes analysis.

11.4 Subject Study Completion and Withdrawal

A subject will be considered completed when the 12-month visit is completed, and all data collection is complete. Subjects who withdraw for any reason will have all available data entered into the database. Reasons for withdrawal will be entered on the Study Exit eCRF.

11.5 Subjects Lost-to-Follow-Up

A subject will be considered LFU from the last missed clinical evaluation if all reasonable efforts made to contact the subject and request their continued participation in the study have failed. All attempts to contact the subject will be documented.

11.6 Confidentiality of Data

Information regarding study subjects will be kept confidential and managed according to the requirements and regulations of the local and national governing bodies and QAPs of Acutus Medical or participating Clinical Research Organizations (CROs).

All data and information collected during this study will be considered confidential by Acutus Medical and their delegates. All data used in the analysis and summary of this study will be anonymous and without reference to specific subject names. Access to subject files will be limited to authorized personnel of Acutus Medical (including core labs), the Investigator, Clinical Site research staff, and authorized Regulatory Authorities. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study.

11.7 Source Documents

Source data encompasses all information, original records of clinical findings, observations, or other activities, which are required in a clinical trial for the reconstruction and evaluation of the trial. Examples of these original documents, and data records include, but are not limited to, hospital records, clinical and office charts, laboratory notes, memoranda, subject diaries or evaluation checklists, recorded data

from automated instruments, copies or transcriptions certified after verification as being accurate and complete, copies of clinic and procedural site coding and billing records, microfiches, photographic negatives, microfilm or magnetic media, X-rays, patient files, and records kept at the pharmacy, and at the laboratories involved in the clinical trial.

Regulations require that the Investigator maintain information in the patient's medical records that corroborate data collected for the study. In order to comply with these regulatory requirements, the following is a list of information that should be maintained, at a minimum:

- Medical history/general physical condition of the subject before involvement in the study, which will be of a sufficient nature to verify the protocol eligibility criteria.
- Study/progress notes, including the date of entry into the study, documenting the following:
  - The general health of the subject.
  - The discussion of the study risks and benefits with the patient.
  - Completion of the ICF process.
  - A statement that the subject reviewed and signed the patient informed consent form.
- Dated notes from each subject visit to support all data recorded on the eCRFs.
- AEs reported and their continuation or resolution at each visit, including supporting documentation, such as discharge summaries, lab results, non-invasive testing reports, etc.
- Notes regarding AADs taken during the study (including start and stop dates, dosage, and routes of administration, if known).
- Subjects general health and medical condition upon completion of, or withdrawal from, the study.

11.8 Electronic Case Report Forms

This study will use an electronic Case Report Form (eCRF) as the primary data collection instrument and will record data by electronic capture. All data requested on the eCRF must be entered within two (2) weeks of the data being generated/collected. All missing data must be explained. If a data entry error has been made, the corrected

information will be entered on the eCRF. All such changes are recorded in the audit and queries reports.

Specific instructions to complete the eCRFs will be provided to the Investigator and other site personnel, as appropriate. The Investigators (and designees) are responsible for reporting clinical study-requested information on the eCRFs.

11.9 Records Retention

The Investigator will retain study essential documents for two (2) years after formal closure or discontinuation of the trial. These documents must be retained for a longer period if required by an agreement with Acutus Medical or defined by local or national regulations. Acutus Medical will inform the Investigator/Institution as to the date of formal closure or discontinuation of the trial.

11.10 Clinical Monitor

A CRO may be designated as the clinical monitor for this study. Their personnel will be qualified by training and experience to oversee the conduct of the study. The Clinical Monitors (also known as Clinical Research Associates (CRAs)) responsibilities include maintaining regular contact with each investigational site through telephone contact or email to ensure that: 1) the CIP/protocol is followed; 2) complete, timely, and accurate data are submitted; 3) problems with inconsistent and incomplete data are addressed; 4) complications and UADEs are reported to the Sponsor; and 5) the site facilities continue to be adequate.

11.11 Clinical Data Monitoring Procedures

Monitoring requirements will be defined in the Clinical Monitoring Plan (CMP). The Clinical Monitors (or designees) may conduct site visits at the study facilities to monitor the study, which will be in compliance with the CIP/protocol, QAPs, and the CMP. When a site visit is performed, the Investigational site agrees to allow the monitors and other authorized Acutus Medical personnel access to information. The monitors may verify data entered into the eCRFs against hospital/clinic records or other source documents in order to ensure accuracy and completeness of the eCRFs for each subject. Clinical Investigators and their staff agree to assist the monitors in their activities. Requests may be made to review patient charts by Acutus Medical personnel and/or designee(s) so that protocol adherence and source documentation can be verified.

Monitoring activities may include, but are not limited to:

- Evaluation of subject screening and selection methods

- Verification of signed informed consent for each subject
- Verification of source documentation against completed case report forms for each subject
- Assurance that required study reports, including reports to the applicable EC, are generated in a timely manner
- Monitoring of Safety Events, including device deficiencies that may have led to an SAE
- Monitoring of device deficiencies, irrespective of associated safety events
- Review of protocol deviations
- Overall study compliance
- Review of the Investigator Site File (ISF)

11.11.1 Medical Monitor

The medical Monitor for the clinical study is:

Andrew Grace, MD
Consultant, Papworth Hospital
Cambridge CB38RE
United Kingdom
Phone: +44 1223 333 631

11.12 Investigator Responsibilities

The investigator is responsible for ensuring that the clinical study is performed in accordance with the protocol, the Declaration of Helsinki, the principles of GCP, International Organization for Standardization (ISO) 14155:2011, applicable regulatory requirements, and institutional procedures.

11.13 Deviations from the Clinical Investigational Plan

A CIP/protocol deviation is defined as an event in which the Investigator or site personnel deviates from the study protocol or study procedures. It is the Investigator's responsibility to ensure that there are no deviations from the protocol. On a rare occasion, a waiver to a screening test, exclusion criteria, or protocol-specific procedure may be granted in advance by Acutus Medical and must be reported in full compliance with all established procedures and conditions of the reviewing EC.

An Investigator may deviate from the protocol without prior written approval from Acutus Medical in cases of medical emergencies to protect the life or physical well-being of a subject. In the event of an emergent deviation, the Investigator is required to notify Acutus Medical and the applicable EC as soon as possible, but no later than five (5) business days from the occurrence of the deviation from the protocol.

Except in such an emergency, prior approval by Acutus Medical is required for changes in, or deviations from, the protocol. Additionally, if these changes or deviations affect the scientific soundness of the investigational plan or the rights, safety, or welfare of human subjects, EC notification is required.

Prior approval is generally not expected in situations where unforeseen circumstances are beyond the Investigator's control (e.g., the subject was not available for a scheduled follow-up office visit or has moved without providing a forwarding address). These events, although outside the Investigator's control, are still required to be reported on the appropriate Protocol Deviation eCRF in order to ensure that all deviations from the standard subject population are adequately documented and reported. The Investigator will inform Acutus Medical and the reviewing EC of all protocol deviations as per the EC requirements established for this study.

If Acutus Medical becomes aware that an Investigator is not complying with the any part of the CIP, including the signed Investigator Agreement (IA), the protocol, or any conditions of approval imposed by the reviewing EC, Acutus Medical will immediately secure compliance, and may suspend the Investigator's participation (including enrollment at the site). Acutus Medical may terminate an Investigator's participation in the study at its discretion.

11.13.1 Maintaining Records

The Investigator will maintain the following accurate, complete, and current records related to the Investigator's participation:

- Correspondence with another Investigator, an EC, Acutus Medical, a Sponsor monitor or designee, or any regulatory agency.
- Records of each patient's case history and exposure to the device, including:
  - Documents evidencing ICF and for participation in the clinical study without informed consent,
  - Any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain ICF,

- All relevant observations, including records concerning adverse device effects (whether anticipated or not),
- Information and data on the condition of each subject upon entering, and during the course of the investigation, including information related to relevant previous medical history and the results of all diagnostic tests,
- A record of the procedure involving treatment with the AcQMap for each subject, including the date and time of the procedure.

- The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

11.13.2 Submitting Reports

In compliance with local and national laws, each Investigator may be required to prepare and submit complete, accurate, and timely reports to Acutus Medical and/or ECs. These reports may include:

- Any UADE occurring during an investigation.
- Any deviation from the CIP/protocol made to protect the life or physical well-being of a subject in an emergency.
- A protocol deviation requiring prior written Acutus Medical approval (except in emergency situations). If the deviation affects the scientific soundness of the plan or the rights, safety, or welfare of subject, prior documentation of EC approval may be required.
- Any further information requested by an EC about any aspect of the investigation.

The Investigator will provide, in writing, any withdrawal of EC approval of the study or an Investigator within five (5) business days of such action.

11.14 Acutus Medical Responsibilities

11.14.1 General Duties

Acutus Medical has the overall responsibility for the conduct of the study, including assurance that the study satisfies the regulatory requirements of the appropriate regulatory agencies, ensuring EC approvals, selecting Investigators, ensuring proper monitoring and that ICF is obtained. Acutus Medical will provide all information necessary to conduct the study, including the CIP/protocol and any reports of prior investigations, as appropriate. During the conduct of the clinical study, updates

regarding information that may impact the clinical study will be made available to all appropriate national and local regulatory authorities.

11.14.2 Selection of Investigators

Acutus Medical will select Investigators (including Sub Investigators performing the procedure) qualified by training and experience. Sites will be selected based on a site assessment, appropriate facilities, clinical experience, and the qualifications of the Principal Investigator (PI). Investigators will be evaluated by Acutus Medical based on:

- Curriculum vitae, or other statement of Investigator's relevant training and experience, including type of experience with the intended procedure and clinical research, specifically.
- Education and experience in the ablation management of arrhythmias
- Whether the Investigator has an adequate patient population to meet requirements of the study enrollment.
- Whether the Investigator has adequate time to be personally involved in the conduct of the study, and adequate research staff and resources to support the study.
- Whether the Investigator's Study Center is associated with an EC that satisfies all applicable regulatory requirements.
- Whether an Investigator was involved in an investigation or other research that was terminated. This may require an explanation of the circumstances that led to the termination.

Prior to study initiation, each Investigator must also submit a:

- Certificate of human patient's protection training (if required by the reviewing EC),
- Signed Investigator's Agreement, indicating an Investigator's commitment to:
  - Conduct the investigation in accordance with the agreement, the CIP/protocol, GCP, and any conditions of approval imposed by the EC;
  - Supervise all testing of the device involving human subjects;
  - Ensure that the requirements for informed consent are met;
  - Conduct the study according to the CIP/protocol.

The Sponsor reserves the right to apply additional criteria to site and/or Investigator selection.

11.15 Training

Acutus Medical will provide training on the AcQMap System **prior** to enrolling any subject. Training may consist of a review of the IFU, hands-on training on the device and procedure, presentations, literature, etc. Additional training will include a review of the protocol, the regulations for medical device investigations, and general study logistics required to complete the study.

Training of appropriate clinical study personnel will be the responsibility of Acutus Medical (or designee). To ensure uniform data collection and protocol compliance, training will include a review the CIP/protocol (including the ICF), techniques for identification of eligible subjects, instructions on data collection, methods for scheduling follow-up visits in the window, etc. Detailed feedback regarding completion of the eCRFs, study requirements, and protocol compliance will be provided by Acutus Medical, its study monitors, and/or designees functioning in a data management capacity.

11.15.1 Changes in the Clinical Investigational Plan

Acutus Medical will obtain appropriate regulatory approval for any change to the CIP/protocol that may affect the scientific soundness of the investigation or the rights, safety, and/or welfare of the subjects.

Acutus Medical will provide approved protocol amendments to the Investigators prior to implementing the amendment. The Investigator will be responsible for notifying the reviewing ECs of the protocol amendment (administrative changes) or obtaining EC approval of the protocol amendment (changes in subject care or safety), according to the instructions provided with the protocol amendment. The EC acknowledgement/approval of the protocol amendment must be documented in writing prior to implementation of the protocol amendment. Copies of this documentation must be provided to Acutus Medical and placed in the Trial Master File (TMF).

11.15.2 Withdrawal of Regulatory Approval

Acutus Medical will notify all reviewing ECs and participating Investigators of any withdrawal of regulatory approval to conduct the clinical study and shall do so within five (5) business days after receipt of notice of the withdrawal of approval.

12 ETHICS AND REGULATORY COMPLIANCE

12.1 Conduct of the Clinical Study

Conduct of the clinical study will follow QAPs from Acutus Medical, as well as the Declaration of Helsinki, GCPs, EN ISO 14155:2011, and other regional and local laws. Each Investigator must sign and date the IA prior to the start of this study. With the signature, the Investigator agrees to perform all study procedures according to the governing local and national regulations and the CIP/protocol.

12.2 Ethics Committee Approval

A properly constituted, valid EC must review and approve the CIP/protocol, ICF, and related patient information and recruitment materials prior to initiation of the study. It is the responsibility of the Investigator to obtain protocol approval from the institution's EC, and to keep the EC informed of any SAEs or SADEs and amendments to the protocol. Additional requirements imposed by the EC or other regulatory authority shall be followed as appropriate. All correspondence with the EC should be filed by the Investigator and copies sent to Acutus Medical (or designee).

12.3 Clinical Study Informed Consent Approval

In accordance with the principles of Informed Consent, the Declaration of Helsinki, GCP, and EN ISO 14155:2011, ICF will be obtained and documented in writing before a patient is enrolled in the clinical study.

It is the responsibility of the Investigator to ensure that a written ICF is obtained from the patient (or legally acceptable representative) before any activity or procedure is undertaken that is not part of routine care. Information obtained during the conduct of the clinical study that may impact the patient ICF may require revisions to the ICF. If so, revisions and approvals of such changes by the appropriate regulatory authority is required. Documentation of the current versions of the informed consent will be documented in the clinical study TMF.

12.4 Identification and Confidentiality

Subject identification and confidentiality will be ensured in accordance with all applicable regulatory and EC governance. This includes, but is not limited to, the following:

- Subjects will be identified on all eCRFs and source documents by a unique anonymized identification reference number.
- eCRFs are confidential documents and will only be made available to Acutus Medical (and appropriate designees), the Investigator, the

biostatistician, and, if requested, to advisory committees and regulatory authorities (including United States Food and Drug Administration (USFDA)).

- Data will be stored in accordance with regulations for handling of electronic data.

Each study site will maintain (anonymous to Acutus Medical) a list identifying all subjects entered into the trial. The list will be maintained as part of the investigation file and monitored for completeness.

12.5 Site Qualification Visits

Site Qualification Visits (SQV) will follow Acutus Medical QAPs.

12.6 Site Initiation Visits

All study personnel will be required to participate in a Site Initiation Visit (SIV) that follows Acutus Medical's QAP. When possible, the SIV training will be completed via a web access meeting. Components of this initiation visit may include:

- Introduction of the study design including the protocol-specific treatment and follow-up phase
- ICF process
- Product training to all end-users
- eCRF completion training
- Safety reporting instructions
- Training on the regulations governing human research
- Procedure training on the use of the device

12.7 Insurance

Acutus Medical shall maintain insurance coverage for this study. Pertinent information regarding the coverage shall be made available to the site upon request.

12.8 Site Audit Plan

Participation as an Investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable compliance and quality assurance offices. The Investigator and/or designee must be available to respond to reasonable requests and queries made by authorized regulatory representatives during the audit process. The Investigator must provide Acutus Medical with copies of all

correspondence that may affect the review of the current study or their qualifications as an Investigator in this and future clinical studies conducted by Acutus Medical.

12.8.1 Site Data Audits by Acutus Medical

In accordance with local and national regulations and Acutus Medical's operating procedures, an internal audit may be requested to access all study records, including source documents, for inspection and duplication. The investigator will ensure the capability for inspections of applicable study-related functions.

Site data quality assurance audits may be conducted at various sites during the clinical study. Selection of sites to undergo auditing will be determined by the Acutus Medical as needed.

12.8.2 External Audits

Requests by regulatory agencies to inspect the study sites may be made as well. The Investigator and/or designee is required to report to Acutus Medical as soon as possible after receiving a request from a regulatory authority to perform an audit. The clinical Investigator agrees to allow inspectors from regulatory agencies to review records and to assist the inspectors in their duties, if requested.

12.9 Public Domain Access to the Clinical Study

A description of this clinical trial will be available on http//www.Clinicaltrials.gov. Information regarding the public access will be presented in the ICF.

12.10 Required Reports

Acutus Medical will remain in compliance with all required and pre-specified reports during the enrollment and follow-up of the clinical study. EC requirements for reports will be provided as requested.

13 GENERAL CONSIDERATIONS

13.1 Discontinuation of the Clinical Study

The Sponsor reserves the right to discontinue the study at any stage, with suitable written notice to the Investigator and the appropriate government regulatory agencies. Similarly, Investigators may withdraw from the study, subject to providing written notification to the Sponsor within thirty (30) days of their intent to withdraw. However, the Sponsor and Investigators will be bound by their obligation to complete the follow-up of subjects already enrolled into the study.

Acutus Medical, as Sponsor, may terminate Investigator and site participation in the study if there is evidence of an Investigator's failure to maintain adequate clinical standards or evidence of an Investigator's or staff's failure to comply with the CIP/protocol.

Notification of suspension or termination will occur no later than five (5) business days after Acutus Medical makes the determination. In the event of study suspension or termination, Acutus Medical or designee will send a report outlining the circumstances to the reviewing EC, the appropriate regulatory agencies, and to all participating Investigators. Any suspension or termination may not be re-initiated without prior approval of the EC and Acutus Medical.

13.2 Use of Information and Publications

All information concerning Acutus Medical operations, patent applications, manufacturing processes, and basic scientific data supplied by Acutus Medical to the Investigator and not previously published, are considered confidential and remain the sole property of Acutus Medical. This includes all study materials, CRF forms, worksheets, and eCRFs.

The information developed in this study may be used by Acutus Medical as support for a regulatory filing and in connection with the continued development of the AcQMap System. Any publication or other public presentation of the data resulting from this study will require prior review and written approval of Acutus Medical.

At the conclusion of the study, it is expected that Acutus Medical and the Investigators will promptly prepare and submit a multi-center manuscript for publication in a reputable scientific journal. The publication of the principal results, including abstracts, from any single-site experience within the study is not allowed until the preparation and publication of the multi-center results. Exceptions to this rule require the prior written approval of Acutus Medical.

Further analyses, beyond those presented in the initial multi-center publication may be proposed to Acutus Medical. Many secondary manuscripts are anticipated. For purposes of timely abstract presentation and publication, such secondary publications may be delegated to the appropriate principal authors; however, final analyses and manuscript review for all multi-center data will require the prior written approval of Acutus Medical.

None of the results, in whole or part, of the study carried out under this protocol, nor any of the information provided by Acutus Medical for the purposes of performing the study, will be published or passed on to any third party without the consent of Acutus Medical. Any Investigator involved with this study is obligated to provide Acutus Medical with complete test results and all data derived from the study.

14 APPENDIX

14.1 Bibliography

A bibliography of pertinent publications identified or supportive of the clinical study will be maintained by Acutus Medical and is available upon request.