Abbott	Clinical Investigation Plan Cover Page

NCT Number: NCT03733392
Advisor HD Grid
Advisor™ HD Grid Observational Study
Study Document No: ABT-CIP-10257
Version B
Date: 25-SEP-2018

Sponsor

Abbott
5050 Nathan Lane North
Plymouth, MN 55442
USA

[redacted]

Clinical Investigation Plan

CRD_932
Advisor HD Grid Observational Study

Version	B
Date	September 25, 2018
Planned Number of Sites and Region(s)	Up to 30 sites Worldwide
Clinical Investigation Type	Prospective, non-randomized, multicenter observational study
Sponsor	Abbott 5050 Nathan Lane North Plymouth, MN 55442 USA
CIP Author of Current Version	[redacted]

[redacted]

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SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

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

Site Principal Investigator

Printed name:
Signature:
Date:

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COMPLIANCE STATEMENT:

This clinical study will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, ISO 14155:2011 standards and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical study will be approved by the appropriate Ethics Committee (EC) of the respective clinical site and as specified by local regulations.

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1 INTRODUCTION

This document is the clinical investigation plan (CIP) for the Advisor HD Grid Observational Study. This clinical study is a prospective, multi-center, observational study intended to quantify and characterize the outcomes of radiofrequency (RF) ablation after, and the utility of electroanatomical mapping with the market-released Advisor™ HD Grid Mapping Cather, Sensor Enabled™ in subjects with persistent atrial fibrillation (PersAF) or ventricular tachycardia (VT) in the real-world environment. This clinical study is sponsored by Abbott.

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

1.1 Background and Rationale

1.1.1 Background

Atrial Fibrillation (AF) is a supraventricular arrhythmia characterized by rapid and irregular activation in the atria, and, when maintained greater than seven days, is known as Persistent AF (PersAF).[1] Patients with PersAF have an increased risk of stroke and are likely to develop life-threatening problems such as tachycardia-induced cardiomyopathy and congestive heart failure which can increase mortality. Restoration and maintenance of sinus rhythm in these patients may confer mortality benefit.[1, 2]

Sustained monomorphic VT is a cardiac arrhythmia emanating from the ventricles at a rate greater than 100 bpm that is sustained longer than 30s or requires intervention due to hemodynamic instability.[3] Sustained VT is associated with increased mortality risk including risk of sudden cardiac death. Patients are often implanted with an implantable cardiac defibrillator (ICD) for treatment when episodes occur, although treatment with an ICD is not curative and is associated with increased mortality and decreased quality of life. Treatment to avoid recurrent symptoms is therefore both desirable and may improve survival in patients.[4]

Catheter ablation is an established treatment option for PersAF and VT, although corresponding success rates in long-term sinus rhythm maintenance remain modest and could benefit from further research. Ablation strategies target the pathogenic mechanisms that initiate and perpetuate abnormal electrical activity within the heart including abnormal substrate. However, identifying and eliminating the pathogenic mechanisms is not straightforward, especially with complex arrhythmias such as PersAF and VT in which the distribution of potential arrhythmogenic drivers is heterogeneous across the patient population and there remains a lack of consensus on approach to identifying and ablating mechanistic drivers.

PersAF is electrophysiologically characterized by fast and regular atrial activities, complex fractionated atrial electrograms, direction of wave front propagation, and low peak-to-peak voltage. Potential drivers of PersAF beyond pulmonary vein triggers may include areas of fibrosis, focal automaticity, or foci, areas of rapidly rotating reentrant circuits, or rotors, asynchronous activation of myocyte bundles identified by complex fractionated electrograms, overactive ganglionated plexi, and dissociation and interaction between epicardial and endocardial layers.[1, 5, 6] The role of such mechanisms continues to be debated along with their implication on therapeutic strategy, especially since ablation techniques aim to eliminate AF triggers or modify arrhythmogenic substrate. Similarly, the majority of patients with sustained monomorphic VT requiring therapy have some type of structural heart disease, and VT associated with

structural heart disease is characterized by scar tissue and slow conduction zones which form a critical isthmus.[4] Multiple techniques are used to both locate such pathologic substrate including identification of local abnormal ventricular activities (LAVA), late potentials, fractionated electrogram signals, and wavefront mapping, and to guide ablation strategies including targeting all LAVA or late potentials, scar homogenization, and dechanneling.[7]

Recent advancements in high-density three-dimensional catheter mapping strategies enable the evaluation of such electrophysiologic characteristics that are used as surrogates for identifying the mechanisms responsible for PersAF and VT.[6, 7] Identification of electrophysiological characteristics depends on the ability of mapping catheter electrodes and electrode pair electrograms to detect voltage characteristics. However, unipolar and/or bipolar EGM amplitudes may be influenced by the direction of the wavefront, catheter orientation, electrode size, interelectrode spacing, proximity to tissue and contamination by far-field signals.[7] Accurate electrogram depiction of underlying substrate is limited by adequate bipole orientation which can be challenging to achieve with traditional linear mapping catheters, noncompliant catheters unable to make adequate tissue contact, and high density mapping catheters with inconsistent electrode spacing. The Advisor™ HD Grid, Sensor Enabled™ (HD Grid) diagnostic mapping catheter with equispaced multipolar grid electrodes provides known bipole spacing in orthogonal directions, thereby providing the ability to discriminate voltage differences in two directions for enhanced directionality and amplitude detection. This is done by using the HD Wave electrode configuration with AutoMap best duplicate enabled during electroanatomical map creation (Appendix V). It is hypothesized that the use of HD Wave mapping will allow high-resolution substrate identification, but the impact of this mapping catheter and configuration on the subsequent ablation strategy used by physicians remains unknown.

1.1.2 Rationale for Conducting this Clinical Study

The HD Grid catheter is a recently launched multielectrode catheter with electrodes evenly distributed in a grid to allow for orthogonal bipole orientations that may overcome current multielectrode catheter limitations. Not much is known about how HD Grid is used clinically in the real world, with published literature including only two case reports.[8, 9] It is hypothesized that electroanatomical mapping with the HD Grid catheter and HD Wave mapping will provide high-density and high-resolution mapping for improved insight to the extent of structural disease and assist in the determination of the “critical” atrial/ventricular targets to guide catheter ablation strategy. This can allow physicians to avoid both unnecessary overtreatment that could result in increased risk of complication, procedure duration, and fluoroscopy exposure, and undertreatment with increased likelihood of recurrence in patients that present with complex arrhythmias.

Therefore, investigation of the new-to-market HD Grid mapping catheter will be useful in elucidating how the high-density, multielectrode catheter and HD Wave mapping configuration are used to identify arrhythmogenic heterogeneous substrate in complex PersAF and VT substrate, guide ablation strategy, and achieve favorable procedural characteristics, while overcoming current limitations to traditional multielectrode catheters.

2 CLINICAL STUDY OVERVIEW

2.1 Clinical Study Objective

The aim of this study is to quantify and characterize the outcomes of radiofrequency (RF) ablation after, and the utility of electroanatomical mapping with the Advisor™ HD Grid Mapping Catheter, Sensor

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Enabled™ (hereafter called "HD Grid") and EnSite Precision™ Cardiac Mapping System (SV 2.2 or higher, hereafter called "EnSite Precision") with HD Wave Vmax voltage mapping (hereafter called "HD Wave") in subjects with PersAF or VT in real-world clinical settings. This will be completed through the assessment of two main objectives which are as follows:

2.1.1 Outcomes Objective:

The first objective is to quantify and characterize the acute- and long-term success rate of RF ablation after electroanatomical mapping with HD Grid and EnSite Precision with HD Wave in subjects with PersAF or VT.

2.1.2 Utility Objective:

The second objective is to quantify and characterize the use of HD Grid and EnSite Precision with HD Wave in the electroanatomical mapping of PersAF or VT in real-world clinical settings.

2.2 Device(s) To Be Used in the Clinical Study

2.2.1 Names of Devices Used in the Study

All devices used in this clinical study must have proper regulatory approval and will be used according to their indications for use and Instructions for Use (IFU).

The devices that will be used in this clinical study are summarized in Table 1.

Table 1. Clinical Study Devices

Device name	Model/Type	Manufacturer
Advisor™ HD Grid Mapping Catheter, Sensor Enabled™	D-AVHD-DF16	SJM
EnSite Precision™ Cardiac Mapping System v 2.2 or later	H702496	SJM
Advisor™ HD Grid Mapping Catheter, Sensor Enabled™ Software Kit *(License entitlement to use HD Grid Catheter with EnSite Precision 2.2)*	H702519	SJM
Sensor Enabled™ Diagnostic Catheter Cable	D-AVSE-CBL22	SJM
EnSite Precision™ Surface Electrode Kit	EN0020-P	SJM
EnSite™ AutoMap Module	H702498	SJM

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Additional commercially available tools may be used in this clinical study, per physician's discretion and per device IFUs.

2.2.2 Intended Indication for Use

Indications for use may be found in the appropriate device IFU. Indications for the use of HD Grid and EnSite Precision are described below.

The Advisor™ HD Grid Mapping Catheter, Sensor Enabled™, is indicated for multiple electrode electrophysiological mapping of cardiac structures in the heart, i.e., recording or stimulation only. This catheter is intended to obtain electrograms in the atrial and ventricular regions of the heart.

The EnSite Precision™ Cardiac Mapping System is a catheter navigation and mapping system capable of displaying the three-dimensional (3D) position of conventional and sensor enabled electrophysiology catheters, as well as displaying cardiac electrical activity as waveform traces and as dynamic 3-D isopotential maps of the cardiac chamber. The contoured surfaces of these three-dimensional maps are based on the anatomy of the patient's own cardiac chamber.

The EnSite Precision™ Cardiac Mapping System (including AutoMap) is a suggested diagnostic tool in patients for whom electrophysiology studies have been indicated.

The EnSite Precision™ system interfaces to either MediGuide™ Guided Medical Positioning System or the EnSite Precision™ Module to combine and display magnetic processed patient positioning and orientation mapping information. When used with an EnSite Precision™ Surface Electrode Kit, the EnSite Precision™ Cardiac Mapping System is intended to display the position of conventional electrophysiology (EP) catheters in the heart.

2.2.3 Description of the Devices Used in this Study

Please refer to the IFU for additional information regarding the devices used in this clinical study.

3 CLINICAL STUDY DESIGN

This is a prospective, non-randomized, multicenter observational study to quantify and characterize the outcomes of RF ablation after, and the utility of electroanatomical mapping with HD Grid and the EnSite Precision with HD Wave in subjects with PersAF or VT in real-world clinical settings. A total of 500 subjects will be enrolled at up to 30 investigational sites worldwide.

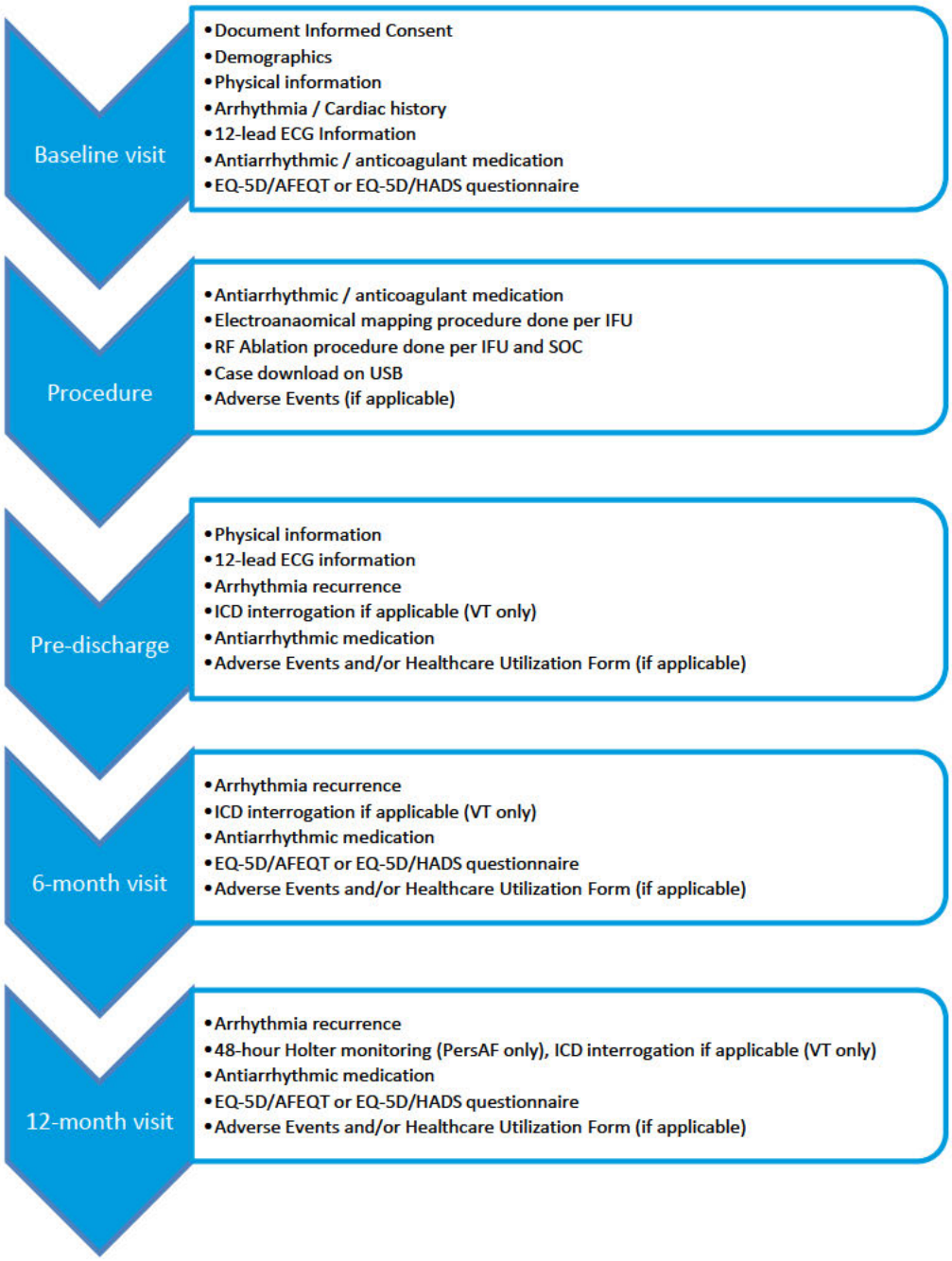
[redacted] Subjects will be followed for up to 12-months after their initial ablation procedure. The outcome and utility descriptive endpoints will be evaluated when all subjects have completed their long-term follow-up visits (12-months for PersAF and 6-months for VT). Additional descriptive endpoints will be evaluated when all subjects have completed their 12-month follow-up visits. [redacted]

3.1 Clinical Study Procedures and Follow-up Schedule

Subjects will be consented for the trial prior to any data collection. Once eligibility is confirmed and a subject is consented, baseline information will be collected and the subject will undergo the RF ablation procedure per physician discretion using electroanatomical mapping with the HD Grid mapping catheter. Subjects will be followed for 12-months post procedure. Follow-up assessments will occur either in person at a clinic or via phone contact after the procedure. The study visits will occur at baseline, [redacted]

procedure, pre-discharge, and 6- and 12-months post ablation procedure. The subject will be exited from the study after completion of the 12-month follow-up visit. The visit schedule and related study assessments are summarized in Figure 1, and further detail provided in section 6.

Figure 1. Clinical Study Flow Chart



3.2 Measures Taken to Avoid and Minimize Bias

Multiple measures will be taken to avoid bias in this clinical study. First, the Advisor HD Grid Observational Study is prospective, such that the outcome of the study is unknown at time of enrollment, and all subjects must meet pre-defined eligibility criteria thereby minimizing selection bias. Next, guidance will be provided to sites regarding data collection for questionnaires and post-procedure follow-up visits and/or phone calls, and case report forms for data collection will be provided to all sites thereby minimizing inter-observer variability. Evaluation of arrhythmia recurrence via Holter monitoring will be performed by an independent core laboratory. Adverse events will be internally assessed by the Sponsor independent of assessment by the physician as reported by the site. Additionally, protocols are in place to minimize subjects lost to follow-up and collection of missing data to minimize the impact or bias caused by missing data.

3.3 Suspension or Early Termination of the Clinical Study

No formal statistical rule for early termination of the clinical study is defined.

The Sponsor reserves the right to discontinue the clinical study at any stage or reduce the follow-up period or sample size with suitable written notice to the investigator.

Should the clinical study be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements.

Should this occur, the investigator shall provide a written statement as to why the premature termination has taken place to the IRB/EC (if applicable). All applicable clinical study documents shall be subject to the same retention policy as detailed in Section 11 of the CIP.

A Principal Investigator, IRB/EC, or regulatory authority may suspend or prematurely terminate participation in the clinical study at the investigational sites for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

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

4 ENDPOINTS

The objectives of this study will be addressed through multiple descriptive endpoints and will be reported using summary statistics. All descriptive endpoints will be evaluated independently for the PersAF and VT subjects.

4.1 Descriptive Endpoint(s)

4.1.1 Outcomes Objective

The first objective is to quantify and characterize the acute- and long-term success rate of RF ablation after electroanatomical mapping with HD Grid and EnSite Precision with HD Wave in subjects with PersAF or VT.

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To quantify and characterize the acute- and long-term success rate of RF ablation after electroanatomical mapping with HD Grid, the following will be summarized:

- Rate of acute success defined as the proportion of subjects who receive HD Grid mapping and RF energy delivery resulting in acute termination of clinical arrhythmia, defined by termination to SR (or AT if being treated for PersAF) or non-inducibility of clinical arrhythmia after ablation (cardioversion allowed prior to inducibility attempt).

- Rate of long-term success defined as the proportion of subjects who receive HD Grid mapping and RF energy delivery with the following pre-defined procedural endpoints:
  Persistent AF (utilizing a 90-day blanking period following index ablation):
  - freedom from all atrial arrhythmias (AF/AFL/AT) greater than 30 seconds (as documented by 48-hr Holter at 12-month follow-up) and new or increased dose of class I/III antiarrhythmic drug (AAD).
  - freedom from all atrial arrhythmias (AF/AFL/AT) greater than 30 seconds (as documented by 48-hr Holter at 12-month follow-up) on or off class I/III AAD.

  VT (utilizing a 14-day blanking period following index procedure):
  - freedom from recurrence of sustained monomorphic VT and new or increased dose of class I/III AAD at 6-month follow-up
  - freedom from recurrence of sustained monomorphic VT on or off class I/III AAD at 6-month follow-up.

    Where recurrence of sustained monomorphic VT is defined as:
    - Sustained monomorphic VT greater than 30s or requiring appropriate ICD pacing or shocks for patient with ICDs
    - Sustained monomorphic VT greater than 30s recorded in follow-up visits or requiring intervention due to hemodynamic instability for patients without ICDs

4.1.2 Utility Objective

The second objective is to quantify and characterize the use of HD Grid and EnSite Precision with HD Wave in the electroanatomical mapping of PersAF or VT in real-world clinical settings.

Use of HD Grid and EnSite Precision with HD Wave will be quantified and characterized through the summary of the following:

- Overall procedure time: defined as time from initial catheter insertion to final catheter removal.
- Radiofrequency (RF) time: defined as duration of time RF energy is delivered
- Fluoroscopy time: defined as total time subject is exposed to fluoroscopy
- Mapping time associated with mapping arrhythmia: defined as the total cumulative mapping time and mapping time for the creation of each map (including any new or retrospective map created with Manual, AutoMap, and TurboMap mapping)
- Number of mapping points collected: defined as total number of mapping points collected for the creation of each map
- Number of mapping points used: defined as the total number of mapping points used in each map
- Number of used mapping points per minute: defined as the total number of mapping points used divided by the relative mapping time
- Substrate characteristics identified: for each type of arrhythmogenic substrate this will be defined as the frequency of substrate type identified in cases that attempted to identify the specific substrate

- Ablation strategy(s) used: defined by both the type of map used to define ablation strategy and the frequency each ablation strategy/target was used by physicians
- Role of HD Wave map relative to along-the-spline map in ablation strategy decision: as assessed by physician survey comparing maps generated with HD Wave electrode configuration to along-the-spline electrode configurations.
- Maneuverability of HD Grid catheter: defined as the ability to maneuver the HD Grid to each specified anatomic location if attempted, the ability to contact cardiac tissue, and the incidence of induced ectopic beats during maneuvering
- HD Grid electrogram quality relative to ablation catheter electrograms: defined as the proportion of electrograms collected with HD Grid that have better quality/less noise than electrograms collected with the ablation catheter at the same cardiac location as assessed by physician survey

4.1.3 Additional descriptive endpoints

Additional descriptive endpoints include:

- Change in quality of life (QOL) at 6 and 12 months after receiving HD Grid mapping and RF ablation relative to baseline: defined as change in quality of life assessed in validated QOL surveys (EQ-5D and AFEQT for subjects with PersAF, EQ-5D and HADS for subjects with VT)
- Rate of periprocedural and immediate post procedural (48hrs) procedure- or device- related adverse events in all subjects in whom the HD Grid is inserted (regardless of RF energy delivery).
- Rate of procedure- or device-related adverse events and cardiovascular serious adverse events in all subjects in whom the HD Grid is inserted (regardless of RF energy delivery) through 30 days post study procedure.
- Proportion of VT subjects who receive HD Grid mapping and RF energy delivery free from recurrence of sustained monomorphic VT and new or increased dose of class I/III AAD, and free from recurrence of sustained monomorphic VT on or off class I/III AADs at 12-month follow-up outside the blanking period.
- Rate of repeat ablations after study procedure during 12-month follow up defined as proportion of subjects without an additional ablation procedure to treat indicated cardiac arrhythmia (outside blanking period, if applicable).
- For subjects treated for PersAF:
    - Proportion with atypical atrial flutter (AFL) identified during procedure
        - Of those receiving HD Grid mapping and RF ablation for AFL: Utility of HD Grid specific to the identification and treatment of atypical AFL (as defined in section 4.1.2), including role of HD wave relative to along-the-spline maps in identifying ablation target(s), and time of RF application to terminate atypical AFL

5 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical study will enroll male and female subjects over the age of 18 years who are indicated for cardiac RF ablation with electroanatomical mapping for the treatment of PersAF or substrate-based VT. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any study-specific procedures not considered standard of care.

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5.2 Subject Screening and Informed Consent

5.2.1 Subject Screening

Members of the site's clinical study team (physician and/or research coordinator, or other delegated and qualified personnel) previously trained to this CIP must screen potential patients for clinical study eligibility based on the inclusion and exclusion criteria (section 5.3) and document the screening effort onto a site-specific Screening Log.

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

Patients who meet all inclusion criteria and none of the exclusion criteria are eligible to participate in this clinical study. Eligible patients presenting at clinical sites will be fully informed about the clinical study and asked to sign an Informed Consent form if they wish to participate in the clinical study. These patients will also be entered into the screening log.

The following assessments may need to be performed after obtaining consent and prior to the procedure, as part of the screening process:

- Pregnancy test
- Intracardiac thrombus assessment

Subject data will be collected for the clinical study after obtaining signed Informed Consent.

5.2.2 Informed Consent

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

The Investigator or his/her authorized designee will conduct the Informed Consent process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical study that are relevant to the subject's decision to participate, such as details of clinical study procedures, anticipated benefits, and potential risks of clinical study participation. Subjects must be informed about their right to withdraw from the clinical study 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 study will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. The subject shall be provided with the Informed Consent form written in a language that is understandable to the subject and has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any study-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

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

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

5.2.3 Vulnerable Populations

Vulnerable patients are defined as patients whose willingness to volunteer in a clinical study could be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples of populations which may contain vulnerable patients include: Individuals with lack of or loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving informed consent. Other vulnerable patients include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the sponsor, members of the armed forces, and persons kept in detention. Enrollment of vulnerable patients in this clinical study is not allowed (exclusion criterion 13).

5.3 Eligibility Criteria

5.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on review of medical records, interview with a candidate patient, and determination by the investigator. If some of the clinical and laboratory tests required to assess eligibility are not performed as part of the sites standard of care, they must be done after written informed consent is obtained. Patients must meet ALL inclusion criteria to be considered for the clinical study. If ANY of the exclusion criteria are met, the patient is excluded from the clinical study.

5.3.2 Inclusion Criteria

1. Subject must provide written informed consent for study participation and willing and able to comply with the protocol described evaluations and follow up schedule
2. Over 18 years of age
3. Indicated for cardiac electroanatomical mapping and RF ablation procedure to treat PersAF or VT
4. Subject is diagnosed with either PersAF *OR* VT as defined by:
    a. Persistent AF:
        i. Documented symptomatic persistent AF defined as continuous atrial fibrillation that is sustained beyond 7 days but less than 12 months
    b. VT:
        i. Sustained monomorphic ventricular tachycardia with record of VT event within last 6 months and history of prior myocardial infarction

5.3.3 Exclusion Criteria

1. Life expectancy less than 12 months

2. Women who are pregnant or nursing
3. Known intracardiac thrombus or myxoma verified within 48 hours of index ablation procedure
4. Myocardial infarction (MI) or unstable angina, or previous cardiac surgery within 60 days of index ablation procedure
5. Percutaneous coronary intervention (PCI) within 30 days of index ablation procedure
6. Documented cerebroembolic event within the past 12 months (365 days)
7. History of valve repair, presence of a prosthetic valve, or severe mitral regurgitation thought to require valve replacement or repair within 12 months
8. Awaiting cardiac transplantation or other cardiac surgery within the next 12 months (365 days)
9. Current acute illness or active systemic infection or sepsis
10. Currently enrolled in another clinical study that could confound the results of this study
11. Any cause for contraindication to ablation procedure or systemic anticoagulation
12. 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 study or to comply with follow-up requirements, or impact the scientific soundness of the clinical study results.
13. Vulnerable patient or individuals whose willingness to volunteer in a study, in the judgement of investigator or public authorities, could be unduly influenced by lack of or loss of autonomy
14. Indication-specific exclusion criteria including:
    a. PersAF:
        i. PersAF felt to be secondary to electrolyte imbalance, uncontrolled thyroid disease, or reversible or non-cardiac cause.
        ii. LAD > 55 mm (parasternal long axis view)
        iii. LVEF < 40%
        iv. Uncontrolled heart failure or NYHA function class III or IV
        v. Presence of implanted ICD/CRT-D.
    b. VT:
        i. VT/VF thought to be from channelopathies
        ii. Active ischemia or other reversible cause of VT
        iii. Incessant VT at time of procedure
        iv. Implanted with a ventricular assist device (VAD) (e.g. TandemHeart)
        v. Chronic NYHA Class IV heart failure
        vi. Ejection fraction < 15%

Incessant VT is defined as continuous sustained VT that promptly recurs despite repeated intervention for termination over ≥3 hours.

5.4 Subject Enrollment

A subject is considered enrolled in the clinical study from the moment the patient provides written informed consent, has been confirmed to meet all inclusion criteria and none of the exclusion criteria, and the HD Grid catheter is inserted.

5.5 Subject Withdrawal

Each enrolled subject shall remain in the clinical study until completion of the required follow-up period; however, a subject's participation in any clinical study is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Subjects will be requested to specify the reason

for the request to withdraw. The investigator must make all reasonable efforts to retain the subject in the clinical study until completion of the clinical study.

Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death
- Subject voluntary withdrawal
- Subject lost-to follow-up as described below

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

No additional follow–up will be required or data recorded from subjects once withdrawn from the clinical study, except for the status (deceased/alive) for up to 30 days post-withdrawal.

5.5.1 Lost-to-Follow-up

If the subject misses any scheduled follow-up visit, attempts at contacting the subject as detailed below will be made within the follow-up visit window. If a subject misses the 6-month follow-up visit it will be considered a missed visit. If the attempts at contacting the subject detailed below are unsuccessful for the 12-month visit, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, a letter (certified if applicable) should be sent to the subject.

[redacted]

6 TREATMENT AND EVALUATION OF ENDPOINTS

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

6.1 Baseline Visit

6.1.1 Baseline/Pre-procedure Clinical Assessments

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

- Documentation of the informed consent process
- Confirmation of enrollment criteria, including pregnancy test if patient is a female of child bearing potential
- Subject demographics
- Complete physical exam including height, weight, 12-lead ECG and NYHA assessment (If these assessments were performed prior to consent, they may be used if they were completed within 60-days of the ablation procedure)
- Echocardiography results (LVEF and LAD assessments) or other means of assessing LVEF and LAD (If these assessments were performed prior to consent, they may be used if they were obtained within 6-months of the ablation procedure)
- Cardiovascular disease history (most recent value prior to baseline visit)
- Arrhythmia history including documentation of PersAF or VT diagnosis (as described in the inclusion criteria)
- Antiarrhythmic medication – including any current class I/III AAD and dose, and history of any class I/III AAD and maximum dose
- Current anticoagulant medication
- Completion of the EQ-5D/AFEQT (for subjects with PersAF) or EQ-5D/HADS (for subjects with VT) questionnaires

Record the required information on the appropriate CRFs. Any protocol deviations (refer to Section 10.5 for details) observed will also be recorded at this time.

[redacted]

6.2 Procedure Visit

The procedure should be performed according to the IFU of the HD Grid mapping catheter, EnSite Precision™ Cardiac Mapping System, and any other medical devices used during the procedure. Physicians performing electroanatomical mapping and ablations must be qualified operators and trained on the study. Each physician who ablates during a particular case needs to be documented on the Procedure CRF.

The following information will be collected during the Procedure Visit:

- Antiarrhythmic medications- any current class I/III AAD and dose
- Anticoagulant medications
- Subject cardiac rhythm when they enter the EP lab
- Subject cardiac rhythm during mapping
- Mapping and ablation tools used during the procedure
- Procedural characteristics (set up and timing)
- Fluoroscopy time
- Mapping time (total time to collect mapping data and time for each map created/ retrospectively generated)
- Mapping points collected and used for each map created/ retrospectively generated
- Mapping location(s)
- Electrode configuration used for clinical electroanatomical mapping
- Map type(s) (i.e. Voltage, LAT, CFE, etc.)
- AutoMap settings used (if applicable)
- Arrhythmogenic substrate identified
- Field Scaling use
- Standard and HD Wave map comparisons
- Ablation strategy
- AutoMark settings used (if applicable)
- Cardioversions performed during procedure
- Attempt(s) at induction of arrhythmia as applicable before and after RF delivery
- Subject rhythm after completion of procedure

The entire case (procedure) must be recorded and stored on a study-specific USB (password-protected), provided by the Sponsor, and returned within a reasonable timeline to the Sponsor.

Protocol deviations (refer to Section 10.5 for details) that were observed during the procedure, which include any device used off-label during the procedure, will also be recorded at this time.

6.2.1 Pre-procedure thrombus assessment

Thrombus assessment is required before procedure and will be performed per investigator's standard of care. If a thrombus is discovered, the procedure should be postponed and the subject placed on anticoagulation until the thrombus is resolved and confirmed by imaging. The subject will not need to be re-consented for the study after the thrombus resolves, provided that the subject continues to meet all eligibility criteria and will undergo an RF ablation procedure unless otherwise indicated by the governing IRB/EC. Baseline visit information should be verified and updated as necessary.

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6.2.2 Electroanatomical mapping

The HD Grid Mapping catheter must be used with EnSite Precision to generate a baseline electroanatomical map prior to ablation procedure. Complete contact with the cardiac wall should be achieved before collecting data. Mapping will be done per investigator discretion and is recommended to use an HD Wave electrode configuration for catheter set-up (see Appendix V). Additional maps may be created or retrospectively generated using TurboMap per physician standard practice for diagnostic purposes.

For comparison of HD wave and along-the-spline electrode configuration maps, any HD Wave configuration map used during the case should also be generated using the along-the-spline electrode configurations, preferably using TurboMap with the same geometry as baseline map (see Appendix V for details on configuration and transitions between map types). This may be done during the diagnostic procedure as part of standard of care procedure flow for relevant comparisons prior to ablation strategy determination. If not performed during the procedure, this should be performed after completion of the ablation procedure for comparison of maps resulting from different electrode configurations. Similarly, any along-the-spline electrode configuration map used during the procedure should have a comparable HD Wave configuration map generated for comparison.

For the purposes of this protocol, creating a map or mapping, is considered to be the process of collecting electroanatomical data points within heart via movement or positioning of the mapping catheter within the heart.

A retrospective map will be defined as the generation of a map that does not require collection of any new or additional electroanatomical data points but instead reuses already collected mapping data with new point collection or acquisition settings or electrode configurations selected (via TurboMap) or manual alteration of a copied open map.

Information related to each map generated, and comparison of any HD wave and respective along-the-spline maps will be reported on the appropriate CRF.

6.2.3 Indication-specific Procedural Recommendations

6.2.3.1 Persistent AF:

Create a baseline geometry and map (at a minimum, collect baseline map, other maps may be collected or retrospectively generated per standard of care) of entire left atrium using HD Grid with HD Wave electrode configuration. Create or retrospectively generate any additional electroanatomical maps (may include generation of maps with along-the-spline configuration, preferably using TurboMap with same geometry; see Appendix V). Use the baseline HD Wave map and/or additional maps as clinically necessary, to identify ablation target(s), and use ablation catheter per IFU to perform ablation per standard of care. Assess acute procedural success. Collect additional maps and perform additional ablation as clinically necessary. Ablation to treat other arrhythmias that occur during the procedure are allowed per physician discretion and standard of care.

If the subject presents in atypical AFL at any time during the procedure or as a result of induction, diagnostic mapping and RF ablation will be allowed. If this occurs, HD Grid with HD Wave electrode configuration should be used to create diagnostic maps per standard of care. Create or retrospectively generate any additional electroanatomical maps (may include generation of maps with along-the-spline configuration, preferably using TurboMap with same geometry; see Appendix V). Use the HD Wave map and/or additional maps as clinically necessary, to identify ablation target(s), and use ablation catheter per

IFU to perform ablation per standard of care. Information related to diagnostic mapping and ablation of the atypical AFL will be collected.

6.2.3.2 VT:

Create a baseline geometry and map (at a minimum, collect baseline voltage map, other maps may be collected per standard of care) of the ventricle(s) using HD Grid with HD Wave electrode configuration. Create or retrospectively generate any additional electroanatomical maps (may include generation of maps with along-the-spline configuration, preferably using TurboMap with same geometry; see Appendix V). Use the voltage HD Wave map, and/or other maps as clinically necessary to identify ablation target(s). Use ablation catheter per IFU to perform ablation per standard of care. Attempt to re-induce any VT ablated if possible. Assess acute procedural success. Create post-ablation voltage map or collect additional maps and perform additional ablation if clinically necessary.

6.3 Pre-discharge Visit (In-hospital)

Prior to discharge after the study procedure, a Pre-discharge visit will be completed. The following information will be collected from each subject at the Discharge Visit:

- 12-lead ECG
- Collect ICD session records and interrogation reports if applicable
- Arrhythmia recurrence
    - For the purposes of this clinical study recurrence of arrhythmia is deemed to have occurred only when the arrhythmia is documented on ICD, ECG, or other monitoring device used per standard of care. Atrial arrhythmias 30 seconds or longer will be collected. Ventricular arrhythmias treated by an ICD, or lasting 30 seconds or longer will be collected
- Antiarrhythmic medications- any current class I/III AAD and dose
- Adverse events if applicable
- Protocol deviations if applicable

6.4 Follow-up Visits

Follow-up visits are scheduled at 6 months and 12 months post procedure. The scheduled visit windows are calculated from the index procedure.

6.4.1 **6-month (180 days ± 90 days) and 12-month (360± 90 days) Visits**

The 6-month follow-up visit may be competed in-clinic or via phone call per investigational site standard of care. The 12-month follow-up visit must be completed in-clinic. The following information will be collected at each visit:

- Arrhythmia recurrence
- Antiarrhythmic medication- including any current class I/III AAD and dose
- Completion of the EQ-5D/AFEQT (for subjects treated for PersAF) or EQ-5D/HADS (for subjects treated for VT)
- Collect ICD session records and interrogation reports if applicable
- Holter monitoring at 12-month visit (for patients treated for PersAF)
    - *Subjects treated for PersAF will be issued a Holter monitor at the 12-month visit and instructed to obtain a 48-hour recording. A core laboratory will review each recording and report findings to the Sponsor.

[redacted]

- Other monitoring device source documentation of arrhythmia if applicable
- Adverse events if applicable
- Document any cardiovascular healthcare utilization performed since the last scheduled study visit as defined in Section 6.4.3 if applicable
- Protocol deviations if applicable

NOTE: The Sponsor may request access to other patient data during the required protocol follow up visits or throughout the follow up period, which may include, but is not limited to, data from implanted device(s).

Record the required information on the appropriate CRF(s). Documentation of arrhythmia (e.g. ECG printouts, Holter printouts, session records) where applicable, should be retrieved and submitted electronically through EDC to the Sponsor.

Sponsor representatives can be involved in providing support during the follow-up procedures.

6.4.2 Unscheduled Visits

If a subject is seen by any physician for possible arrhythmia recurrence and/or arrhythmia associated symptoms outside of a regularly scheduled study visit and/or had an urgent care or emergency room visit regarding possible arrhythmia, these visits need to be documented as “Unscheduled Visits”. Minimally, the following information should be documented for an unscheduled visit.

- 12-lead ECG, if performed during the visit
- ICD session records and interrogation reports if applicable
- Other monitoring device source documentation of arrhythmia if applicable
- Antiarrhythmic medication- including any current class I/III AAD and dose
- Occurrence of any repeat ablation
- Document adverse events and cardiovascular healthcare utilization if applicable
- Protocol deviations if applicable

6.4.3 Healthcare Utilization Documentation

Healthcare utilization for cardiac-related hospitalizations (inpatient or outpatient), emergency room visits, and/or urgent care visits will be documented in this clinical study. Subjects will be interviewed at each scheduled visit to determine if they had any cardiac-related hospitalizations (inpatient or outpatient), emergency room visits, and/or urgent care visits since their last scheduled visit. Source documentation for these visits should be obtained and a Healthcare Utilization form completed.

6.4.4 Patient Reported Outcome Measures – Quality of Life Questionnaires

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

The following patient-reported outcome measures will be collected for the respective patient populations:

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

[redacted]

- EuroQol Five Dimensions Questionnaire (EQ-5D)
- Hospital Anxiety and Depression Scale (HADS)

6.4.5 Schedule of Events

The schedule of activities specific to this clinical study are described in the preceding sections and are summarized in Table 2.

Table 2. Clinical Study Specific Tests/Activities and Procedures

Visit / Study Activity	Time of Consent (may be at time of baseline visit)	Baseline Visit(s)	Procedure Visit	Pre-discharge	6-month Visit (180 days ± 90 days post procedure)	12-month Visit (360 days ± 90 days post procedure)	Unscheduled Visit
Eligibility check	X	(X)	(X)				
Informed Consent	X						
Demographics		X					
Physical examination		X					
LVEF and LAD assessment		X					
Cardiovascular Disease History		X					
Arrhythmia History		X					
12-Lead ECG		X		X	(X)	(X)	(X)
Anticoagulant Medication		X	X				
Antiarrhythmic Medication		X	X	X	X	X	(X)
EQ-5D/AFEQT or EQ-5D/HADS questionnaires		X			X	X	
Mapping of cardiac structures and electroanatomical map(s)			X				
RF Ablation			X				
Obtain Procedure USB			X				
48-hour Holter-monitoring (PersAF only)						X	(X)
ICD interrogation (VT only)				(X)[a]	(X)[a]	(X)[a]	(X)[a]
Other arrhythmia monitoring and source documentation					(X)	(X)	(X)
Healthcare Utilization					(X)	(X)	(X)
Repeat Ablation				(X)	(X)	(X)	(X)
Protocol Deviation	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Adverse Events	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Death	(X)	(X)	(X)	(X)	(X)	(X)	(X)

(X) If applicable
[a] Non-SJM ICDs may require in-office interrogation

6.5 Core Laboratory

A core lab will be used for the collection, interpretation, and collation of data collected from Holter monitoring.

[redacted]

The core lab will provide independent review of this data by appropriately trained personnel using standardized procedures to interpret Holter monitor tracings for adjudication of atrial arrhythmias. Findings will be communicated to the investigator and to Abbott. The core lab's adjudication findings will be used for analysis.

7 ADVERSE EVENTS

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

7.1 Definitions

7.1.1 Adverse Event

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

Note 1: This definition includes events related to the medical device(s) used in this study.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to medical devices used in this study.

7.1.2 Serious Adverse Event

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

a) Led to a death,

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

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

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

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

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7.2 Device Relationship

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

7.2.1 Adverse Device Effect (ADE)

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

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

7.2.2 Serious Adverse Device Effect (SADE)

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

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

7.3 Safety Reporting

7.3.1 Adverse Event Reporting

Safety surveillance and reporting starts for each subject as soon as the subject is enrolled in the clinical study and will continue until the subject's 12-month follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical study, or the subject withdraws from the clinical study. All device effects regardless of severity (ADEs and SADEs) and cardiovascular SAE data, will be collected throughout the time period defined above and will be reported to the Sponsor on the Adverse Event CRF. Additional information with regard to an adverse event and death should be updated within the appropriate CRF.

Recurrence of AF, AFL, or AT in subjects treated for PersAF or recurrence of VT in subjects treated for VT are not considered reportable adverse events unless they occur in severity, frequency, or other manner that is significantly worse than the subject's baseline condition. Recurrence of arrhythmia will be reported as part the descriptive endpoints and will be reported on the Follow-Up Visit CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

7.3.2 SAE Reporting

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

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

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

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

7.3.3 Complaints

During the study, the investigator will be responsible for reporting all complaints they became aware of. A complaint is defined as any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a device after it is released for distribution.

The investigator must notify the Abbott Product Performance Group (PPG) by submitting the information on the device via email to AF_ProductSurveillance@abbott.com or by phone 651-756-5400 as soon as possible after becoming aware of the complaint. This information will not be collected on a CRF for the study.

The Sponsor will investigate all complaints according to the Sponsor's post market surveillance/customer complaint procedures and will report it to the appropriate regulatory body if necessary

8 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical study. The study will investigate the outcomes of RF ablation after, and the utility of electroanatomical mapping with HD Grid and EnSite Precision with HD Wave. The study is a prospective, multicenter, unblinded observational study.

Endpoints described in Section 4.1 will be analyzed and reported using summary statistics. No hypothesis tests will be performed. Additional analysis using data collected in this study, including data from the recorded EnSite Precision case, may be performed during or after completion of the 12-month follow-up period for all subjects.

A one-sided 0.025 level of significance or two-sided 0.05 level of significance will be used to declare statistical significance, as applicable. Multiplicity adjustments will not be made unless specified below.

Statistical analysis will be performed using SAS version 9.3 or higher, or other analysis tools/software as necessary.

8.1 Analysis Populations

[redacted]

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A safety analysis population will be used for safety-related descriptive endpoints. All subjects who have signed informed consent and have the HD Grid catheter inserted will be included in the safety analysis population regardless of protocol violations, as this is the most conservative analysis.

8.2 Statistical Analyses

8.2.1 Descriptive endpoints

The endpoints for evaluating the main study objectives are described in section 4.1.

8.2.2 Analysis Methodology

The endpoints will be summarized descriptively based on available data or measurements in the analysis population. No formal hypothesis testing will be performed.

In general, continuous variables will be summarized with the numbers of observations, means with standard deviations, quartiles, minimums, maximums, and 95% confidence intervals for the means as per the table mockups.

Categorical variables will be summarized with subject counts and percentages/rates, and where specified in the table mockups, with exact 95% Clopper-Pearson confidence intervals.

All pre-defined adverse events will be captured. Only adverse events that occur after HD Grid catheter is inserted (after enrollment) will be analyzed, as defined in the safety analysis population. Tables will be created that show incidences of all ADEs. Cardiovascular serious adverse events will be analyzed and reported in a similar manner as ADEs.

Survival analysis will be conducted to analyze time-to-event variables. Events occurring during the 90 days following the ablation procedure for PersAF subjects (90-day blanking period) or 14-day blanking period following the ablation procedure for VT subjects will not be counted as an effectiveness outcome failure. Subjects without events will be censored at their last known event-free time point. Subjects withdrawn or otherwise lost-to-follow-up during the follow-up period will be censored at their last known visit. Survival data will be presented using the Kaplan-Meier product limit method.

[redacted]

8.4 Timing of Analysis

Data analyses will be performed at the completion of the 12-month follow-up period for all subjects or as desired by Sponsor.

In addition, study progress and data may be summarized and reported as needed.

8.5 Subgroup Analysis

There are no pre-specified subgroup analyses planned for this clinical study. Although, all descriptive endpoints will be analyzed separately for PersAF and VT populations.

[redacted]

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8.6 Multiplicity

No hypothesis testing will be performed; therefore, no adjustments will be made for multiplicity in the endpoint analyses.

8.7 Procedures for Accounting for Missing Data

Every effort will be made to collect all required data. All data available for the endpoints specified among the analysis population will be used. Missing data will not be imputed. Kaplan-Meier analysis will censor subjects withdrawn or otherwise lost-to-follow-up at last known visit.

8.8 Planned Interim Analysis

An interim analysis of acute descriptive endpoints related to the use of HD Grid and the Precision system with HD Wave will be performed when 250 subjects have been enrolled and completed the procedure visit and related data collection.

8.9 Statistical Criteria for Termination

There are no statistical criteria for termination of this clinical study.

8.10 Success Criteria

Pass/Fail criteria do not apply to this study.

8.11 Deviations from Statistical Plan

Any major changes or less significant changes to the planned statistical analyses will be documented in the final report.

8.12 Analysis of Baseline Data

Tables will be created to define the study population at baseline. Tables will include demographics, physical examination, cardiac history, arrhythmia history, 12-lead ECG, antiarrhythmic/anticoagulant medication use, and QOL data.

8.13 Analysis of Quality of Life

The EQ-5D/AFEQT questionnaires will be analyzed for subjects treated for Persistent AF, and the EQ-5D/HADS questionnaires will be analyzed for subjects treated for VT. Data will be assessed at baseline and then at 6 and 12 months. Data will be compared at each assessment interval to the baseline score.

8.14 Poolability Assessment

An analysis will be conducted to determine if there is a site bias on descriptive endpoint analyses including acute-and long-term outcomes, procedure time, RF time, fluoroscopy time, and mapping time. Sites enrolling small (one through five) and moderate (six through 15) numbers of subjects will be pooled

into small and moderate enrollers and sites enrolling large (more than 15) numbers of subjects will be included in the analysis as individual sites.

9 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

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

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

10 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

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

10.2 CIP Amendments

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

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

10.3 Training

10.3.1 Site Training

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

10.3.2 Training Required for the Use of the Device

All investigators involved in the conduct of this clinical study will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately. Each physician participating in the study procedure must have experience using HD Grid and EnSite Precision for PersAF and/or VT treatment prior to participation in the study.

10.4 Monitoring

It is the responsibility of the Sponsor to ensure the clinical study is conducted, recorded and reported according to the approved CIP, subsequent amendment(s), applicable regulations and guidance documents.

Centralized monitoring will occur through routine internal data review. This monitoring is designed to identify missing and inconsistent data, data outliers, and potential CIP deviations that may be indicative of site non-compliance. On-site monitoring may occur at the discretion of the Sponsor.

10.5 Deviations from CIP

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

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

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

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

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

10.6 Quality Assurance Audit

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

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

10.7 Committees

10.7.1 Publications Committee

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

11 DATA HANDLING AND RECORD KEEPING

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

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 study, 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, if requested.

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

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical study. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data. Confidentiality of data will be observed by all parties involved at all times throughout the clinical study. All data will be secured against unauthorized access.

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11.2 Data Management Plan

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

11.3 Source Documentation

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

- Medical history/physical condition of the subject before involvement in the clinical study sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical study referencing the Sponsor, CIP number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- CIP-required laboratory reports and 12-lead ECGs, reviewed and annotated for clinical significance of out of range results (if applicable). It is acceptable to have labs and/or ECGs reviewed and annotated in the electronic medical record system for site's that have these capabilities. For those sites that do not have such capability, the labs and ECGs should be printed and signed by the investigator.
- Notes regarding CIP-required and prescription medications taken during the clinical study (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical study
- Any other data required to substantiate data entered into the CRF

11.4 Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF completion. The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports. Data on CRFs will be collected for all subjects that are enrolled into the clinical study.

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

11.5 Record Retention

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

12 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

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

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

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

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

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

13 CLINICAL STUDY CONCLUSION

The clinical study will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical study closure.

14 PUBLICATION POLICY

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

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Publications or presentations of clinical study methods or results will adhere to Sponsor's publication policy, which is based on Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines. A copy of the policy will be provided upon request of the investigator. Investigators will be notified via email about the dissemination of study data and opportunities for involvement as authors on publications/presentations.

The Sponsor will be responsible for determining whether to register the clinical study on www.clinicaltrials.gov or any other clinical trials, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. In the event Sponsor determines that the clinical study should be registered, Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical study.

15 RISK ANALYSIS

The risks associated with HD Grid mapping system can be found in the appropriate Instructions for Use. The clinical study does not require additional procedures or assessments beyond what could be considered standard of care. There are no additional risks introduced to subjects due to participation in this study.

15.1 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Refer to applicable IFU for list of Anticipated Adverse Device Effects. There may be risks related to the devices used in this study that are unknown at present. Likewise, the exact frequency of the risk may be unknown.

15.1.1 Risks Associated with Participation in this Clinical Study

Risks to subjects enrolled in this clinical study include those risks currently associated with other commercially available electrophysiology diagnostic procedures and RF catheter ablation procedures. The risks of the procedure are related primarily to mechanical injury to the heart and vessels from catheter manipulation and thermal injury due to RF current delivery, including the risk of thromboembolism and myocardial perforation, especially for ablations in the left atrium.

For those procedures where the physician applies sedation or anesthesia, the standard risks of anesthesia also exist and include allergic reactions, pneumonia, aspiration pneumonitis, atelectasis, prolonged sedation, other medical complications and in very rare cases, death.

15.1.2 Steps Taken to Control or Mitigate Risks

Every possible effort will be taken to minimize the risks, including:

- Careful selection of experienced Investigators for the study
- Training of Investigators and other applicable site personnel on the CIP
- Conducting the clinical study in accordance with the CIP, all applicable laws and regulations and any conditions of approval imposed by the appropriate IRB/EC or applicable regulatory authorities where the clinical study is performed
- Preparation of the all devices in accordance with device IFU, and conducting the ablation procedures in accordance with the IFU of corresponding devices

15.2 Possible Interactions with Concomitant Treatments

There are no known interactions with concomitant treatments.

15.3 Anticipated Benefits

The aim of this study is to quantify and characterize the utility and outcomes of ablation after electroanatomical mapping with HD Grid and EnSite Precision with HD Wave in subjects with PersAF or VT in real-world clinical settings.

The information collected in this clinical study will be added to the current knowledge and understanding of high-density electroanatomical mapping and treatment options for patients with arrhythmias. Subjects participating in this clinical study are not expected to experience any additional benefit or harm compared to patients who are not participating in this clinical study as the clinical study will follow local standard practice.

15.4 Risk to Benefit Rationale

Use of HD Grid mapping system to facilitate electroanatomical mapping in the heart is believed to not introduce any unanticipated risks compared to current practice. Catheter ablation is a recognized safe and effective treatment of cardiac arrhythmias.

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APPENDIX I: ABBREVIATIONS AND ACRONYMS

Acronym/Abbreviation	Description
AAD	Antiarrhythmic drug
AE	Adverse event
AF	Atrial fibrillation
AFEQT	Atrial Fibrillation Effect on QualiTy of Life
AFL	Atrial flutter
AT	Atrial tachycardia
CEC	Clinical Events Committee
CIP	Clinical investigation plan
CRF	Case report form
CRT-D	Cardiac resynchronization therapy defibrillator
DMP	Data Management Plan
EC	Ethics Committee
ECG	Electrocardiogram
EDC	Electronic data capture
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICD	Implantable cardioverter defibrillator
ICF	Informed Consent form
IFU	Instructions for Use
IRB	Institutional Review Board
LAD	Left atrial diameter
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
NYHA	New York Heart Association
PCI	Percutaneous coronary intervention
PV	Pulmonary vein
PVI	Pulmonary vein isolation
QOL	Quality of Life
RF	Radiofrequency
SAE	Serious adverse event
SE	Sensor enabled
SOC	Standard of Care
TIA	Transient ischemic attack
UADE	Unanticipated adverse device effect
VT	Ventricular tachycardia

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APPENDIX II: CASE REPORT FORMS

The Final CRFs will be kept under a separate cover and are available upon request.

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APPENDIX III: SITE CONTACT INFORMATION

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

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APPENDIX IV: INFORMED CONSENT FORM

A template informed consent form will be provided under a separate cover and will be available upon request.

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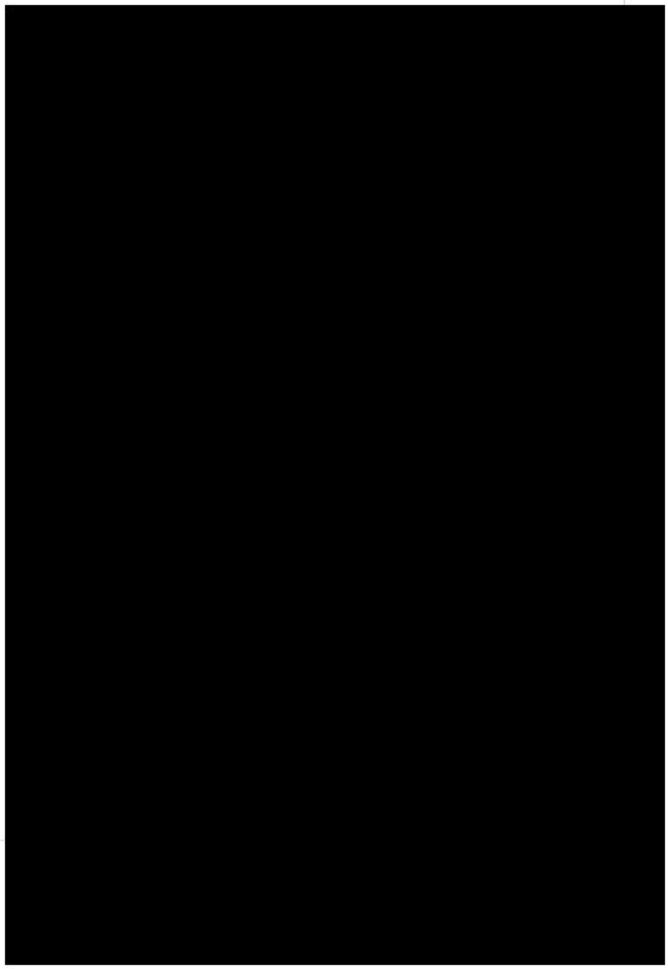

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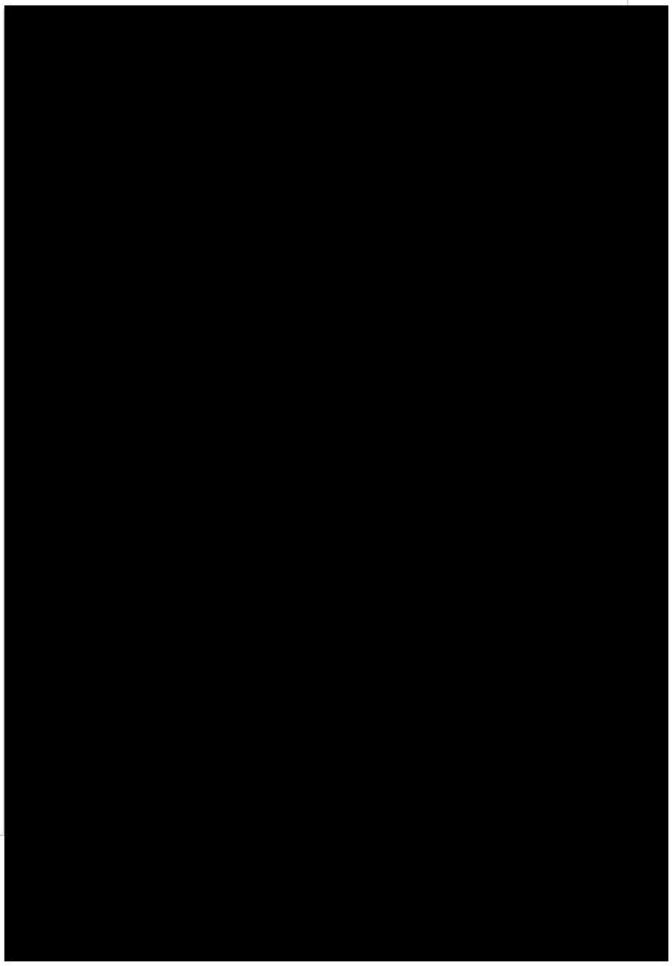

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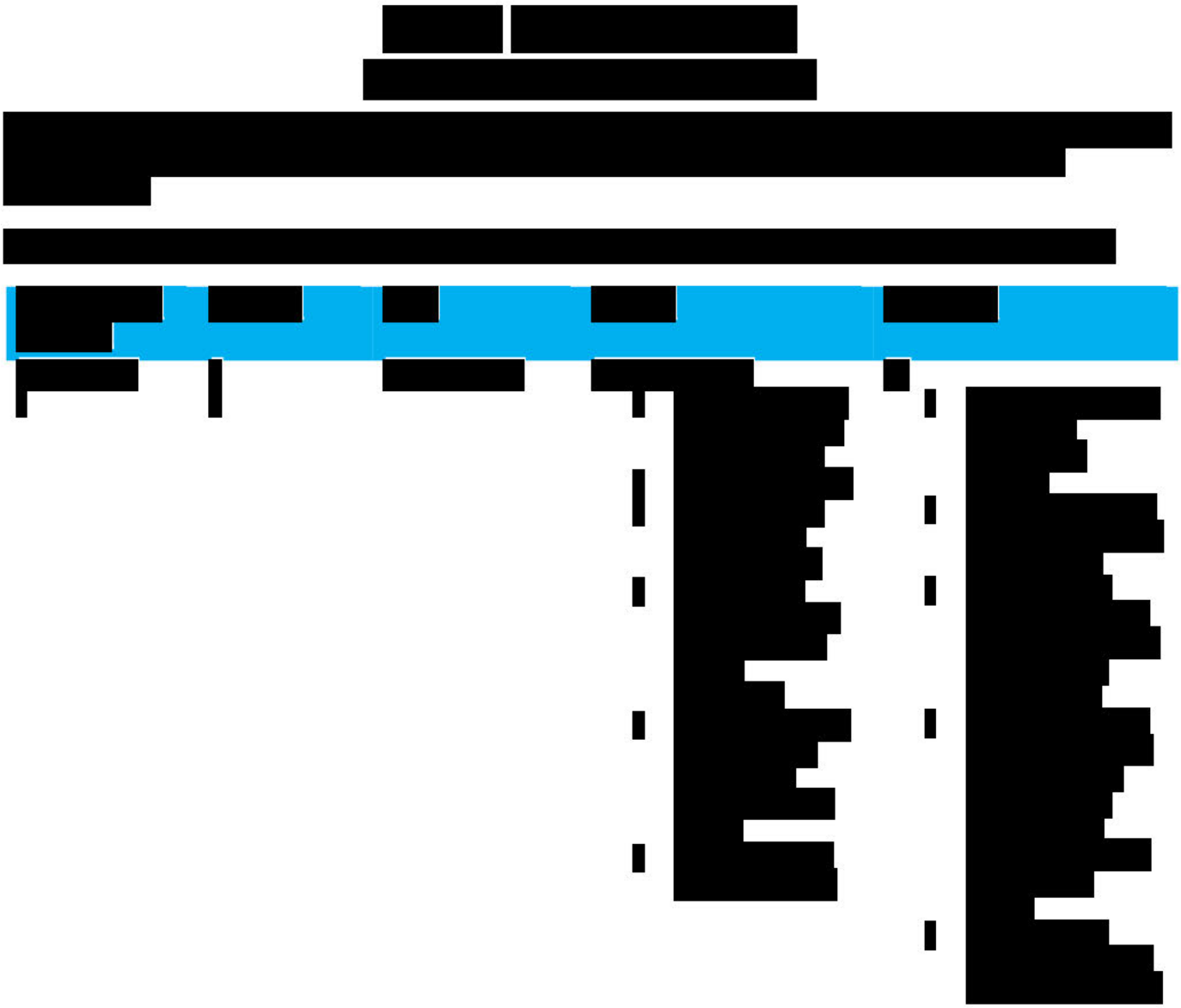

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