STATISTICAL ANALYSIS PLAN

for

DIAMOND-AF Clinical Study (Study Protocol TP00599)

A Randomized Controlled Clinical Evaluation of the DiamondTemp™ Ablation System for the Treatment of Paroxysmal Atrial Fibrillation (DIAMOND-AF)

TABLE OF CONTENTS

1. INTRODUCTION

This statistical analysis plan (SAP) outlines the data and procedures used for assessing the efficacy and safety endpoints of Protocol TP00599: A Randomized Controlled Clinical Evaluation of the DiamondTemp™ Ablation System for the Treatment of Paroxysmal Atrial Fibrillation.

2. STUDY ENDPOINTS

The working hypotheses for this study are that the investigational arm will be non-inferior to the control arm in effectiveness (section 2.1) and safety (section 2.2).

2.1. Primary Effectiveness Endpoint

The primary effectiveness endpoint is defined as freedom from documented atrial fibrillation (AF), atrial flutter* (AFL) and atrial tachycardia (AT) episodes following the blanking period (3-month follow-up post-ablation procedure) through the end of the effectiveness evaluation period (12-month follow-up post-ablation procedure).

An effectiveness failure is defined by any of the following events:

- Inability to isolate all accessible targeted pulmonary veins during the ablation procedure
- Documented episodes of AF, AFL or AT lasting ≥ 30 seconds in duration as evidenced by electrocardiographic data during the effectiveness evaluation period
- DC cardioversion for AF, AFL or AT during the effectiveness evaluation period
- A repeat ablation procedure to treat AF, AFL or AT during the effectiveness evaluation period
- Use of a new or modification to existing Class I-IV anti-arrhythmic drug (AAD) regimen to treat AF, AFL or AT recurrence during the effectiveness evaluation period
- Use of a non- study device for ablation of any AF targets during the index or repeat ablation procedure during the blanking period
- More than one (1) repeat ablation procedures during the blanking period

* *Occurrence and/or ablation of cavotricuspid isthmus (CTI)-dependent AFL, as confirmed by entrainment maneuvers during EP testing at any time during this study is not a primary effectiveness failure because it is not considered an iatrogenic arrhythmia following a left atrial ablation procedure for AF.*

2.2. Primary Safety Endpoint

The primary safety endpoint is defined as freedom from a composite of serious adverse events (SAE) occurring within 30-days and clinically symptomatic pulmonary vein stenosis through 6- months post-index ablation procedure, as adjudicated by an independent Clinical Events Committee (CEC) for relatedness to the procedure or device.

The primary safety device- or procedure-related SAE composite will be the combined rate of the following events*:

- Atrioesophageal fistula
- Bleeding complication
- Cardiac tamponade/perforation
- Death
- Extended hospitalization
- Myocardial infarction
- Pericarditis
- Phrenic nerve paralysis
- Pulmonary edema
- Pulmonary vein stenosis
- Stroke post-ablation
- Thromboembolism
- Transient ischemic attack (TIA) post-ablation
- Vagal nerve injury
- Vascular access complications

* *The primary safety device- or procedure-related SAE events are defined in the DIAMOND-AF Investigational Plan.*

2.3. Secondary Endpoints

Secondary endpoints to characterize the performance of the DiamondTemp Ablation System, relative to the control device, will include:

- Mean duration of individual RF ablations (seconds)
- Mean cumulative RF time per procedure (minutes)
- Freedom from a composite of SAE occurring within 7-days post-index ablation procedure as adjudicated by an independent CEC for relatedness to the procedure or device.
- Freedom from documented AF, AT and AFL* episodes following the

blanking period through 12-month follow-up post-ablation procedure in the absence of class I and III anti-arrhythmic drug therapy.

- Rate of acute procedural success, defined as confirmation of electrical isolation of PVs via assessment of entrance block at least 20 minutes following the last ablation around the respective PV.
- Rate of single procedure success defined as the rate of patients treated with one single ablation procedure during study participation and with freedom from documented AF, AT and AFL* at 12 months.
- Rate of single procedure success defined as the rate of subjects treated with one single ablation procedure during study participation and with freedom from ALL primary effectiveness endpoint failure criteria.
- Rate of occurrence of electrically reconnected PVs following a 20-minute waiting period assessed by entrance block at index procedure.
- Accumulated changes in QOL using the AF QOL Survey (AFEQT Questionnaire) from baseline through 6- and 12-months following ablation procedure.
- Neurological changes measured using the NIH stroke scale between baseline and post- ablation (pre-discharge visit) and at 12 months post-ablation procedure.
- Total procedure time (minutes), defined as time of first assigned ablation catheter insertion into the vasculature to time of last procedural ablation catheter removed.
- Time to achieve initial PVI at index procedure (minutes), defined as time of delivery of first RF ablation with the assigned ablation catheter until confirmation of PVI.
- Total treatment device time (minutes), defined as time of delivery of first RF ablation with the assigned ablation treatment catheter to removal of the treatment catheter.
- Total number of RF ablations per procedure.
- Total fluid infused through the assigned ablation catheter (mL).
- Total fluoroscopy time (minutes).
- Number of re-hospitalizations due to atrial fibrillation recurrence after blanking period.

* *Occurrence and/or ablation of cavotricuspid isthmus (CTI)-dependent AFL, as confirmed by entrainment maneuvers during EP testing at any time during this study is not a primary effectiveness failure because it is not considered an iatrogenic arrhythmia following a left atrial ablation procedure for AF.*

3. STUDY DESIGN AND PROCEDURES

The DIAMOND-AF study is a prospective, single-blind, 1:1 randomized, controlled trial being performed at multiple centers in the United States, Canada and Europe to evaluate the safety and effectiveness of the DiamondTemp Ablation System for the treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation (PAF) compared to the TactiCath Quartz Contact Force Ablation Catheter and compatible ablation system.

This study will enroll up to 480 subjects diagnosed with PAF at up to 30 investigational sites in the US, Canada and Europe. Investigational sites will have a principal investigator (PI) that is responsible for the conduct of a research study as well as sub-investigators. It is anticipated that approximately 50% of the randomized subjects will be enrolled at centers within the United States.

After providing consent, subjects will undergo screening and baseline tests. Subjects that meet the eligibility criteria will be randomly assigned to either treatment with the investigational or control device only after completion of all screening and eligibility procedures. A randomization module within the Electronic Data Capture (EDC) system will be used to randomize subjects 1:1 to one of two treatment groups using a blocked randomization stratified by site followed by stratification by failure of Class I/III or Class II/IV AADs. Since full eligibility for the study may not be confirmed without pre-ablation procedure testing (e.g., echocardiography, pregnancy test, creatinine), consented subjects will count towards the maximum enrollment ceiling once final eligibility is confirmed and they are randomized. Once randomized, a subject will be considered enrolled in the study.

The primary focus of the left atrial ablation procedure is to create a series of point-by-point RF lesions encircling the left and right PVs to achieve electrical PVI from the rest of the left atrium (LA). Investigators may use their preferred approach to obtain PVI, such as antral or WACA ablation targeting PVs segmentally or PV pairs ipsilaterally. PVI must be confirmed by entrance block at least 20 minutes following the last ablation around the respective PV. Targeting non- PV foci and complex fractionated electrograms is not recommended in this investigation. If the investigator identifies additional focal or macro-reentrant atrial sites to be clinically relevant to AF and requiring ablation, the ablation location will be documented.

All subjects will be followed per protocol in relation to the date of the index ablation procedure. Follow up will be required prior to hospital discharge and at 7 days, 1 month, 3 months, 6 months and 12 months post-ablation.

Subjects will be given a cardiac event monitor (Sentinel Wireless ECG Recorder System or equivalent, HeartcoR Solutions, LLC.) at the hospital pre-discharge visit to be used throughout the duration of the study. If subject exhibits symptoms (e.g. palpitations, dizziness, tiredness, lightheadedness, shortness of breath, chest pain, fatigue, syncope) associated with AF recurrence at any time after the ablation procedure, they will be instructed to record their heart rhythm using their cardiac event monitor and to contact the site investigator. This data will be transmitted to and read at an ECG core lab. If a subject has an arrhythmia recurrence within the first 90 days after the ablation procedure

(blanking period), one repeat ablation procedure is allowed per protocol. Investigators should make every attempt to schedule a repeat ablation procedure on or before day 90. The repeat ablation procedure must be performed with the assigned investigational or control catheter. Repeat ablation procedures performed with a catheter different than originally assigned will be a protocol deviation.

The duration of the study is projected to span approximately 36 months. The duration accounts for:

- Approximately 12-15 months to enroll all subjects in the trial;
- Approximately 12 -15 months subject participation from consent to end of 12-month follow-up visit window;
- Approximately 3-6 months to analyze, report on study results and close the study.

4. INTERIM ANALYSES

No formal interim statistical analyses are planned.

5. ANALYSIS POPULATIONS

5.1. Intention-to-Treat Analysis Set

The Intention-to-Treat (ITT) population will be comprised of all randomized subjects regardless of whether they receive study treatment, with analyses conducted according to the randomized treatment assignment.

5.2. Per Protocol Analysis Set

The Per Protocol analysis set will be a subset of the ITT Set and comprised of all subjects who did not have any major protocol deviations (e.g. eligibility criteria deviation and subject not treated in accordance with the randomized treatment assignment).

5.3. Safety Analysis Set

In the unlikely case where a subject is randomized but the procedure is prematurely halted and no catheter is deployed, said subject will be included in the ITT Set but excluded from the Safety Set since the subject was not exposed to the study device. The Safety Set will be comprised of all randomized subjects in which treatment was at least attempted (assigned treatment catheter inserted into vasculature), with analyses conducted by actual treatment received.

6. DEFINITION OF VARIABLES

6.1. Baseline

The last value recorded prior to exposure to study device.

6.2. Study Day Calculation

Study Day 0 is the day of study device deployment.

Study Day is calculated relative to Study Day 0 and will appear in the listings where applicable.

Study Day will be calculated as:

Study Day = (Date of Event – Date of Study Device Deployment)

7. STATISTICAL METHODS

7.1. General Statistical Considerations

The DIAMOND-AF study is a prospective, single-blind, 1:1 randomized, controlled trial being performed at multiple centers in the United States, Canada and Europe.

The randomization for this trial is blocked with a 1:1 ratio and stratified by site followed by stratification by failure of Class I/III or Class II/IV AADs.

If applicable, the following general comments pertain to the statistical analyses and data presentations:

- All statistical analyses will be performed using a two-sided hypothesis test at the overall 5% level of significance. P-values will be rounded to three decimal places. If a p-value is less than 0.001 it will be reported as "< 0.001." If a p-value is greater than 0.999 it will be reported as "> 0.999." No adjustments for multiplicity are planned.
- Continuous data will be summarized using descriptive statistics: n, mean, standard deviation or standard error, median, minimum and maximum. The decision to use either standard deviation or standard error will be based upon the objective of the presentation: standard deviation will be used when the interest is the natural variability of the data; standard error will be used when comparing two or more means. Continuous variables that are recorded using approximate values (e.g., < or >) will be replaced by the closest exact value for the calculation of summary statistics.
- Categorical variables will be summarized using frequency counts and percentages.
- For ordinal-scaled variables, a combination of the above may be employed as appropriate: frequency and percentage of observations within a category and means and standard deviations of the scores of the categories.
- For categorical and ordinal variables, percentages will be calculated based on non- missing data.
- As noted in Section 6.1, baseline is defined as the last measurement for the outcome of interest obtained before the exposure to the study device.
- Duration variables will be calculated using the general formula: [(end date – start date) +1]
- All tables and listings will have a header showing the Sponsor name ("EPIX

Therapeutics" or "EPIX"), the protocol number and the page number with the total number of pages in the listing or table. A footer will show the data extraction date, the file name, path, the program run date, along with notes and definitions for abbreviations used in the tables and listings.

- Within-subject changes will be calculated as visit value minus baseline value such that a negative change reflects a decrease and a positive change signifies an increase. No judgment ("better" or "worse") is associated with the sign of the change, only direction. The paired sample t-test or Wilcoxon Signed Rank test may be used to test the null hypothesis that the mean (or median) within-subject change is equal to zero.
- MedDRA Version 20.0 or higher will be used for coding of all adverse events; WHO-Drug will be used for coding concomitant medications.
- Version 9.2 or higher of SAS® statistical software package or other validated statistical software will be used to provide all summaries, listings, graphs, and statistical analyses.

7.2. Determination of Sample Size

With a randomization ratio of 1:1 and an estimated attrition rate of 7%, 240 subjects per treatment group (total N=480) should yield sufficient power for both the primary safety and primary effectiveness endpoints.

For primary safety, assuming a Control composite SAE rate of 6.5%, 226 subjects per group yields 80% power to detect a non-inferiority margin of 6.5% between treatment groups at a significance level of 0.025. Similarly, assuming a Control effectiveness rate of 65%, 229 subjects per group yields 80% power to detect a non-inferiority margin of -12.5% between treatment groups at a significance level of 0.025.

7.3. Missing Data

The potential biases created by missing data are largely dependent upon their abundance and timing, and such drop-out bias would potentially distort the planned analysis. The employment of any methodology to minimize the impact of early terminations will likely be data-driven during the analyses. One such methodology is Multiple Imputation (MI), whereby each missing datum is replaced by multiple values in multiple datasets. The datasets are conventionally analyzed and the multiple results are combined to yield statistically valid inferences with estimated uncertainty. SAS/STAT provides three models of imputation (regression, propensity scores, and Markov chain); selection of the model of choice will largely depend on the pattern of missing data. Covariates may include site, sex, and age and will be defined prior to the acquisition of outcome data to be modeled.

Subjects in a small pivotal trial conducted at specialty centers are not likely to be lost to follow-up, particularly in an elderly population. Consequently, there should be little missing data and documenting the clinical outcome and vital status of all

subjects and the specific reasons for any premature withdrawal will be feasible. Nevertheless, sensitivity analyses, including tipping point analyses, of the primary safety and effectiveness endpoints may be conducted using several imputation approaches.

8. STATISTICAL ANALYSES

8.1. Subject Disposition

The number and percentage of subjects randomized to either catheter will be summarized (ITT Set) and the number and percentage of subjects treated with either catheter (Safety Set) will be summarized by treatment group. Variables summarized may include total study duration, study completion status, and the primary reason for study discontinuation.

8.2. Eligibility, Demographic and Baseline Characteristics

The following analyses will be performed on the ITT, Per Protocol, and Safety Analysis populations.

8.2.1. Eligibility Criteria

Inclusion and Exclusion criteria will be summarized by treatment group. A summary of any pre-approved Inclusion and Exclusion criteria waivers will be presented.

8.2.2. Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by treatment group. Demographic variables include age, sex, and geographic ancestry. Baseline characteristics include height, weight, BMI, and duration of disease.

8.2.3. Medical and Surgical History

Medical and Surgical History will be summarized by treatment group. Any past medical findings or surgical procedures will be summarized.

8.2.4. Physical Examination at Baseline

The pre-treatment physical exam will be summarized by treatment group.

8.3. Concomitant Medication

All medications taken from the screening date up to the index procedure and after the randomized treatment procedure through the last study visit will be summarized based on the World Health Organization (WHO) Drug dictionary.

8.4. Primary Endpoint Analyses

The primary endpoint analysis will be performed using the ITT Set. The working hypotheses are that the Investigational (INV) arm will be non-inferior to the Control (CTRL) arm in effectiveness and safety. Accordingly, the corresponding statistical hypotheses are presented below:

- Non-inferior Effectiveness: Freedom from documented atrial fibrillation (AF), atrial flutter (AFL) and atrial tachycardia (AT) episodes following the blanking period (3-month follow-up post-ablation procedure) through the end of the effectiveness evaluation period (12-month follow-up post-ablation procedure)
  - H_0: $\pi_{INV} \leq \pi_{CTRL} - \delta$
  - H_1: $\pi_{INV} > \pi_{CTRL} - \delta$

  where π is the population proportion for the corresponding treatment group and δ is the non-inferiority margin of 12.5%.
- Non-inferior Safety: Freedom from a composite of serious adverse events (SAE) occurring within 30-days and clinically symptomatic pulmonary vein stenosis through 6- months post-index ablation procedure, as adjudicated by an independent Clinical Events Committee (CEC) for relatedness to the procedure or device.
  - H_0: $\pi_{INV} \leq \pi_{CTRL} - \delta$
  - H_1: $\pi_{INV} > \pi_{CTRL} - \delta$

  where π is the population proportion for the corresponding treatment group and δ is the non-inferiority margin of 6.5%.

  Additional analyses may be conducted to analyze the primary effectiveness endpoint, such as time-to-first event survival analysis.

8.4.1. Analytical Methodologies

8.4.1.1. Non-Inferior Effectiveness

Non-inferiority of effectiveness rates in the INV arm compared to the CTRL arm will be assessed by use of Farrington-Manning non-inferiority exact tests.

8.4.1.2. Non-Inferior Safety

Non-inferiority of safety event rates in the INV arm compared to the CTRL arm will be assessed by use of Farrington-Manning non-inferiority exact tests.

8.4.2. Per Protocol and Safety Analyses Populations

All of the above primary analyses performed on the ITT population will be replicated using the Per Protocol and Safety Analysis populations.

8.4.3. Homogeneity of Treatment Effect

The following homogeneity analyses will be performed on the ITT, Per Protocol, and Safety Analysis populations.

8.4.3.1. Homogeneity of Treatment Effect Across Study Sites

To evaluate homogeneity of treatment effect (safety and effectiveness primary endpoints), Cochran- Mantel-Haenszel methods will be employed with dimensions of success/failure, Test/Control, and Sites. Low enrollment centers (less than 4 subjects) may be pooled by region (EU vs US/CAN) to form two quasi-sites. A significance level of 0.15 will be used as a threshold for the Breslow-Day test of homogeneity.

8.4.3.2. Homogeneity of Treatment Effect Between DiamondTemp Unidirectional and Bidirectional Catheters

Within the DiamondTemp test group, the treatment effect (safety and effectiveness) between unidirectional and bidirectional catheters sub-groups will be evaluated using contingency table methods, with the dimensions of success/failure and unidirectional/bidirectional. A significance level of 0.15 will be used as a threshold for homogeneity/heterogeneity (e.g., Chi-square or Fisher's exact test). Upon demonstration of homogeneity, the primary analyses will aggregate the two directionality subgroups; if the two subgroups are heterogeneous, the primary analyses will be stratified.

8.4.3.3. Homogeneity of Treatment Effect Between DiamondTemp Generators

Within the DiamondTemp test group, the treatment effect (safety and effectiveness) between the two generator subgroups (model CEDTG100 and model CEDTG200) will be evaluated using contingency table methods, with the dimensions of success/failure and model CEDTG100/model CEDTG200. A significance level of 0.15 will be used as a threshold for homogeneity/heterogeneity (e.g., Chi-square or Fisher's exact test).

8.4.3.4. Homogeneity of Treatment Effect Between DiamondTemp Unidirectional and Bidirectional Catheters Across Generators

Within the DiamondTemp test group, the treatment effect (safety and effectiveness) between unidirectional and bidirectional catheters across the two generator types (model CEDTG100 and model CEDTG200) will be evaluated using Cochran-Mantel-Haenszel methods, with the dimensions of success/failure, unidirectional/bidirectional and model CEDTG100/model CEDTG200. A significance level of 0.15

will be used as a threshold for the Breslow-Day test of homogeneity.

8.5. Secondary Endpoint Analyses

Four specific secondary endpoints will be evaluated for superiority over Control. The analytical approach is one of *a priori* hierarchical hypotheses, with the pre-specified order of the endpoints as follows:

1. Mean duration of individual RF ablations (seconds)
2. Mean cumulative RF time per procedure (minutes)
3. Total fluoroscopy time (minutes)
4. Total procedure time (minutes), defined as time of first assigned ablation catheter insertion into the vasculature to time of last procedural ablation catheter removed.

The first secondary endpoint (i.e., RF ablation time) needs to be significant at the two-tailed α- level of 0.05, before the next one can be considered at the same threshold. Once an endpoint is determined to be non-significant, testing stops and any remaining endpoints are not considered.

Two-sample t-tests will be utilized to compare the two treatment groups on these four pre-specified secondary endpoints. The generalized statistical hypotheses are as follows:

H_0: the population means for the respective Test and Control groups are not different.

H_1: the population means for the respective Test and Control groups are different.

The following secondary endpoints will be analyzed descriptively without hypothesis testing:

1. Freedom from a composite of SAE occurring within 7-days post-index ablation procedure as adjudicated by an independent CEC for relatedness to the procedure or device.
2. Freedom from documented AF, AT and AFL episodes following the blanking period through 12-month follow-up post-ablation procedure in the absence of class I and III antiarrhythmic drug therapy.
3. Rate of acute procedural success, defined as confirmation of electrical isolation of PVs via assessment of entrance block at least 20 minutes following the last ablation around the respective PV.
4. Rate of single procedure success defined as the rate of patients treated with one single ablation procedure during study participation and with freedom from documented AF, AT and AFL at 12 months.

5. Rate of single procedure success defined as the rate of subjects treated with one single ablation procedure during study participation and with freedom from ALL primary effectiveness endpoint failure criteria.
6. Rate of occurrence of electrically reconnected PVs following a 20-minute waiting period assessed by entrance block at index procedure.
7. Accumulated changes in QOL using the AF QOL Survey (AFEQT Questionnaire) from baseline through 6- and 12- months following ablation procedure.
8. Neurological changes measured using the NIH stroke scale between baseline and post- ablation (pre-discharge visit) and at 12 months post-ablation procedure.
9. Time to achieve initial PVI at index procedure (minutes), defined as time of delivery of first RF ablation with the assigned ablation catheter until confirmation of PVI.
10. Total treatment device time (minutes), defined as time of delivery of first RF ablation with the assigned ablation treatment catheter to removal of the treatment catheter.
11. Total number of RF ablations per procedure.
12. Total fluid infused through the assigned ablation catheter (mL).
13. Number of re-hospitalizations due to atrial fibrillation recurrence after blanking period.

* *Occurrence and/or ablation of cavotricuspid isthmus (CTI)-dependent AFL, as confirmed by entrainment maneuvers during EP testing at any time during this study is not a primary effectiveness failure because it is not considered an iatrogenic arrhythmia following a left atrial ablation procedure for AF.*

For binary variables such as freedom rates or procedural success, counts, percentages and exact 95% confidence intervals using Clopper-Pearson's method will be calculated. For continuous variables, means, standard deviations and 95% confidence intervals will be calculated.

8.6. Safety Analyses

8.6.1. Study Discontinuation Due to Adverse Event

Subjects who experienced adverse events leading to discontinuation from the study will be summarized in a tabular form. The following information will be presented for each subject: treatment group, termination date, date of last visit, duration in study (in days), onset and stop dates of the adverse event resulting in treatment discontinuation, MedDRA System Organ Class (SOC) and Preferred Term (PT) and relationship to study procedure or device.

8.6.2. Adverse Events

Adverse event classifications and the respective definitions are described in the Clinical Investigational plan.

An overall summary of reported adverse events (AEs) will be presented by treatment group and will include the number and percentage of subjects who report at least one adverse event, the total number of adverse events, the number of unique adverse events and the number and percentage of subjects who report adverse events by strongest relationship to study treatment and study ablation procedure. The unit of analysis is 'subject' for all adverse event tables, therefore a subject reporting the same adverse event more than once will be counted once when calculating the number and percentage of subjects with that particular event. If a subject reports the same adverse event more than once or has the same adverse event on multiple occasions, the strongest relationship to the study treatment and study ablation procedure. recorded for the event will be presented.

The frequencies and percentages of adverse events will be presented by MedDRA system organ class (SOC) and preferred term (PT) for each treatment group. The frequencies and percentages of AEs judged by the investigator to be at least possibly related to study treatment will be presented by MedDRA SOC and PT. Similar tables will present the same results for the subset of serious adverse events (SAEs).

Complete subject listings of all adverse events will be provided. For each adverse event the following will be specified: treatment group, start and stop dates, MedDRA SOC and PT, relationship to study treatment, relationship to study procedure, action taken, outcome of the adverse event and seriousness (yes/no).

8.6.3. Serious Adverse Events

All serious adverse events will be included in listings and will be summarized in tables by treatment arm.

9. VALIDATION REQUIREMENTS

All data analyses for the clinical study report (CSR) will be validated. Levels of validation required for the different elements of the CSR are specified in the table below.

Validation Level	Definition	Required for
Level I	A peer reviewer independently programs output and then compares the output with that generated by the original author of the program to be validated	All analyses in the CSR pertaining to the primary safety and effectiveness endpoints of the study
Level II	A peer reviewer reviews the program, and where appropriate, performs calculations or programming checks to verify the output	All other analyses in the CSR *

**At a minimum, Level II validation will be performed.*

REVISION HISTORY

Revision	Description of Change	DCO#	Effective Date	Initials
A	Initial release.	0791	08/02/2018	CM
B	Clarify secondary endpoints: From "Mean cumulative RF time (minutes)" to "Mean cumulative RF time per procedure (minutes)"; from "Mean duration of RF ablations (seconds)" to "Mean duration of individual RF ablations (seconds)". Added treatment effect for DiamondTemp Bidirectional Catheter and CEDTG200 generator to Section 8.7 and 8.8.	0928	11/15/2019	CM
C	The Statistical Analysis Plan (SAP) for the Diamond-AF Clinical Study provided to FDA in G170227 S005 has been revised to address FDA's study design consideration. To specifically address the FDA feedback, section 8.4.3.4 was added to document how the interaction between catheter types and generator models on clinical outcomes will be tested using the Breslow-Day test of homogeneity of odds ratio for contingency tables, with differences in clinical outcome (success/failure), catheter type (unidirectional/bidirectional), stratified by generator type (CEDTG100/CEDTG200).	1110	09/30/2019	ED

Revision	Description of Change	DCO#	Effective Date	Initials
D	The Statistical Analysis Plan (SAP) for the Diamond-AF Clinical Study has been revised to align with the Clinical Investigational Plan revisions, as discussed during the 20-FEB-2020 FDA/Medtronic teleconference.	1595	04/01/2020	KF