Statistical Analysis Plan

Post-Market Real World Outcomes in WATCHMAN FLX™ Pro Left Atrial Appendage Closure (LAAC) Device

HEAL-LAA

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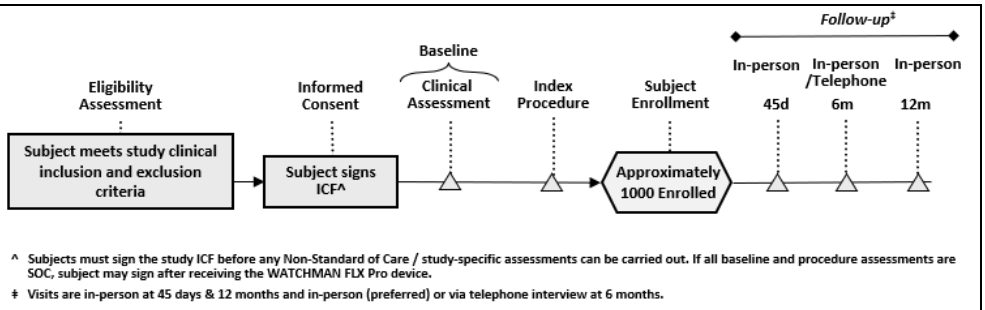
1 PROTOCOL SUMMARY

Study Objective(s)	The primary objective of this study is to collect real-world outcomes data on WATCHMAN FLX™ Pro Left Atrial Appendage Closure (LAAC) Device in patients who are implanted with the WATCHMAN FLX Pro device in a commercial clinical setting.
Indication(s) for Use	As per the product Instructions for Use (IFU), WATCHMAN FLX Pro is intended to reduce the risk of thromboembolism from the left atrial appendage in subjects with non-valvular atrial fibrillation who: • *Are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc scores;* • *Are deemed by their physicians to be suitable for oral anticoagulation (OAC); and have an appropriate rationale to seek a non-pharmacologic alternative to OAC, taking into account the safety and effectiveness of the device compared to OAC*
(Commercial) Device/System applied as Standard of Care and sizes, if applicable	Commercially available WATCHMAN FLX Pro Left Atrial Appendage Closure Device sizes 20mm, 24mm, 27mm, 31mm, 35mm, and 40mm. **Note 1:** The WATCHMAN FLX™ Pro LAAC Device comes preloaded on the WATCHMAN FLX™ Pro Delivery Catheter. The preloaded delivery system is used in conjunction with a commercially available WATCHMAN® Access System (access sheath and dilator)*. *Specific WATCHMAN® Access System devices of interest for the treatment of non-valvular atrial fibrillation may be added as they become commercially available as defined in the Enrollment Guide(s).
Study Design	HEAL-LAA is a prospective, post-market, single-arm, multicenter trial evaluating safety and device success of the WATCHMAN FLX Pro device in subjects with non-valvular atrial fibrillation (AF). A patient is considered enrolled once an approved informed consent form has been signed, all clinical inclusion and no clinical exclusion criteria have been met, and the WATCHMAN FLX Pro device has been used for treatment and/or attempted to be used for treatment. Follow-up clinical assessment and imaging (Transesophageal Echocardiography (TEE)) will occur at 45 days (± 15 days) and 12 months (365 ± 30 days) following implant and will be assessed by an independent core laboratory. Clinical follow-up will be conducted at 45 days (± 15 days), 6 months (180 ± 30 days), and 12 months (365 ± 30 days) post index procedure. The study design is summarized below.

	 **HEAL-LAA Study Design Overview**
Planned Number of Subjects	Approximately 1000 subjects in whom a WATCHMAN FLX Pro device is implanted or attempted to be implanted will be enrolled. Four planned subset analyses will be conducted: • Primary Analysis Subset: Initial 500 enrolled subjects • Access System Subset • Diversity Subset • Full Enrollment Set (all enrolled subjects)
Planned Number of Sites /Countries	Up to 60 investigational centers in the United States.
Primary Efficacy Endpoint	The rate of leak >5 mm at 45-day post-implant TEE for the HEAL LAA primary analysis subset is less than a performance goal (PG).
Primary Safety Endpoint	For the evaluable cohort, the composite rate of all-cause mortality, all stroke, systemic embolism, and major bleeding at 6 months for the HEAL LAA primary analysis subset is less than a performance goal (PG).
Additional Endpoints	The individual components of the composite safety endpoints above will be reported separately in addition to the overall composites. The following events will also be analyzed: • Cardiovascular/unknown death • Non-cardiovascular death • Disabling and non-disabling stroke • Ischemic stroke and hemorrhagic stroke • International Society on Thrombosis and Haemostasis (ISTH) major and non-major clinically significant bleeding o Procedural bleeding and non-procedural bleeding • Device related thrombus • Pericardial effusion/tamponade requiring pericardiocentesis or surgery • Device implant success
Method of Assigning Patients to	The study is a single arm study. All patients enrolled in the study will receive/attempt to receive the WATCHMAN FLX Pro device.

Treatment	
Follow-up Schedule	Study procedures and follow-up visits will occur as follows: • WATCHMAN FLX Pro implant procedure • 45-day follow-up to include TEE imaging (45 ± 15 days post implant) • 6-month follow-up (180 ± 30 days post implant) • 12-month follow-up to include TEE imaging (365 ± 30 days post implant) Subjects who are enrolled but not implanted with a WATCHMAN FLX Pro device (attempted implant only) will be followed for safety through 12 months after the initial attempted index procedure. Attempted implant subjects will not undergo protocol required imaging assessments. The study will be considered complete after all available enrolled subjects have finished the 12-month follow-up visit.
Study Duration	Enrollment is expected to be completed in approximately 6 months; therefore, the total study duration is estimated to be approximately 18 months.
Participant Duration	The study duration for each subject is expected to be approximately 12 months.
Inclusion Criteria	Inclusion criteria are listed below. IC1. Subject is of legal age to participate in the study. IC2. Subject has documented non-valvular atrial fibrillation (i.e., atrial fibrillation in the absence of moderate or greater mitral stenosis or a mechanical heart valve). IC3. Subject is clinically indicated for and is treated or attempted to be treated with a WATCHMAN FLX Pro device. IC4. Subject or legal representative is able to understand and willing to provide written informed consent to participate in the study. IC5. Subject is able and willing to return for required follow-up visits and examinations.
Exclusion Criteria	Exclusion criteria are listed below. EC1. Subject has a documented life expectancy of less than 6 months. EC2. Subject is currently enrolled in another investigational study, except if the subject is participating in a mandatory governmental registry, or a purely observational registry with no associated treatment. EC3. Intracardiac thrombus is present. EC4. An atrial septal defect repair or closure device or a patent foramen ovale repair or closure device is present. EC5. The LAA anatomy will not accommodate a Closure Device. EC6. The patient has known hypersensitivity to any portion of the device

	material or the individual components such that the use of the WATCHMAN FLX Pro device is contraindicated. EC7. Any of the customary contraindications for other percutaneous catheterization procedure (e.g., patient size too small to accommodate TEE probe or required catheters) or conditions (e.g., active infection, bleeding disorder) are present. EC8. There are contraindications to the use of anticoagulation therapy, aspirin, or P2Y12 inhibitor. EC9. Subject is of childbearing potential and is, or plans to become, pregnant during the time of the study (method of assessment per study physician's discretion).
Adjunctive Pharmacologic Therapy	Subjects should be treated with one of the two IFU recommended pharmacologic regimens (OAC+ASA or DAPT) following WATCHMAN FLX Pro implantation.
Statistical Methods	
Analysis Sets	Analysis sets for the study are listed below. - Intention-To-Treat (ITT): This population includes all subjects who sign an Informed Consent Form, meet all clinical inclusion and no clinical exclusion criteria, and are implanted with the study device or attempted to be implanted with the study device. - Implanted: This population includes all subjects who sign an Informed Consent Form, meet all clinical inclusion and no clinical exclusion criteria, and who are implanted with the study device in the correct anatomical position.
Primary Efficacy Endpoint Statistical Hypothesis	The rate of leak >5 mm at 45-day post-implant TEE for the WATCHMAN FLX Pro primary analysis subset is less than a performance goal (PG).
Statistical Test Method for the Primary Efficacy Endpoint	A one-sample z-test will be used to test the one-sided hypothesis that the primary efficacy endpoint rate for the WATCHMAN FLX Pro primary analysis subset is less than a PG: H_0: $P_{WM\_Leak} \geq PG$ H_1: $P_{WM\_Leak} < PG$ where P_{WM_Leak} is the primary efficacy endpoint rate for the WATCHMAN FLX Pro primary analysis subset and PG is the performance goal. The analysis set for the primary efficacy endpoint is the implanted analysis set from the primary analysis subset.
Sample Size Parameters for the	The sample size calculation for the primary efficacy endpoint is based on the following assumptions. • Expected rate for WATCHMAN FLX Pro < 2% (based on historic

Primary Efficacy Endpoint	studies of FLXibility and PINNACLE FLX) • Testing margin = 3% • PG = 5% = expected rate (2%) + testing margin (3%) • 1-sided significance level (α) = 0.025 • Power (1 minus ß) > 85% • Number of evaluable subjects = 400 • Expected attrition rate = 20% Primary analysis subset enrollment for the study = 500 subjects
Success Criteria for the Primary Efficacy Endpoint	If the *P* value from the one-sample z-test is <0.025, the rate of the primary efficacy endpoint for the WATCHMAN FLX Pro primary analysis subset will be concluded to meet the PG. This corresponds to the one-sided upper 97.5% confidence bound on the observed rate of the primary efficacy endpoint being less than the PG.
Primary Safety Endpoint Statistical Hypothesis	For the evaluable cohort, the composite rate of all-cause mortality, all stroke, systemic embolism, and major bleeding at 6 months for the WATCHMAN FLX Pro primary analysis subset is less than a performance goal (PG).
Statistical Test Method for the Primary Safety Endpoint	A one-sample z-test will be used to test the one-sided hypothesis that the 6-month primary safety endpoint rate for the WATCHMAN FLX Pro primary analysis subset is less than a PG: H0: $P_{Safety} \geq PG$ H1: $P_{Safety} < PG$ where P_{Safety} is the primary safety endpoint rate for the WATCHMAN FLX Pro primary analysis subset and PG is the performance goal. The analysis set for the primary safety endpoint is the ITT analysis set from the primary analysis subset. This endpoint will also be analyzed for the implanted analysis set.
Sample Size Parameters for the Primary Safety Endpoint	The sample size calculation for the primary safety endpoint is based on the following assumptions. • Expected rate for WATCHMAN FLX Pro < 14% (based on historic data from FLXibility and PINNACLE FLX) • Testing margin = 7% (50% relative to the expected rate) • PG = 21% = expected rate (14%) + testing margin (7%) • 1-sided significance level (α) = 0.025 • Power (1 minus ß) > 95% • Number of evaluable subjects = 485 • Expected attrition rate = 3% Primary analysis subset enrollment for the study = 500 subjects
Success	If the P value from the one-sample z-test is <0.025, the rate of the primary

Criteria for the Primary Safety Endpoint	safety endpoint for the WATCHMAN FLX Pro primary analysis subset will be concluded to meet the PG. This corresponds to the one-sided upper 97.5% confidence bound on the observed rate of the primary safety endpoint being less than the PG.

2 INTRODUCTION

This statistical analysis plan (SAP) addresses the planned analyses for the clinical study entitled "Post-Market Real World Outcomes in WATCHMAN FLX™ Pro Left Atrial Appendage Closure (LAAC) Device" (HEAL-LAA), based on the approved protocol version B. Approximately 1000 consented subjects will be enrolled. Data for subjects receiving the WATCHMAN FLX Pro device will be collected over 12 months.

3 ENDPOINT ANALYSIS

Four planned subset analyses will be conducted:

- Primary analysis subset: Initial 500 enrolled subjects
- Access system subset
- Diversity subset
- Full enrollment set (all enrolled subjects)

3.1 Primary Efficacy Endpoint

The following hypothesis tests are only based on the primary analysis subset.

3.1.1 Hypotheses

The objective of the primary efficacy endpoint analysis is to test the null hypothesis that the rate of leak >5 mm at 45-day post-implant core-lab TEE for the WATCHMAN FLX Pro primary analysis subset is greater than or equal to 5%. A one-sample z-test will be used to test the one-sided hypothesis.

H_0: $P_{WM\_Leak} \geq 5\%$

H_1: $P_{WM\_Leak} < 5\%$

3.1.2 Sample Size

The sample size was estimated based on the following assumptions:

- Expected rate for WATCHMAN FLX Pro < 2% (based on historic studies of FLXibility and PINNACLE FLX)
- Testing margin = 3%
- PG = 5% = expected rate (2%) + testing margin (3%)
- 1-sided significance level (α) = 0.025
- Power (1 minus ß) > 85%

- Number of evaluable subjects = 400
- Expected attrition rate = 20%

Given the above assumptions, 500 subjects of primary analysis subset will be required.

3.1.3 Statistical Methods

The primary analysis subset with a completed 45-day follow-up TEE will be eligible for inclusion in this endpoint analysis. The primary analysis subset with core lab-completed 45-day TEE will be included in the denominator for the primary effectiveness event rate. The primary analysis subset with core lab-completed 45-day TEE and demonstrated leak >5mm will be included in the numerator. A one-sample z-test will be used to test the assumption that the rate of leak >5 mm at 45-day post-implant TEE is ≥5%. The null hypothesis will be rejected if the resulting p-value is less than 0.025.

3.2 Primary Safety Endpoint

The primary safety endpoint is the composite rate of CEC-adjudicated all-cause mortality, all stroke, systemic embolism, and major bleeding at 6 months. The following hypothesis tests are based on the primary analysis subset.

3.2.1 Hypotheses

The objective of the primary safety endpoint analysis is to test the null hypothesis that the composite rate of CEC-adjudicated all-cause mortality, all stroke, systemic embolism, and major bleeding at 6 months for the WATCHMAN FLX Pro primary analysis subset is greater than or equal to the performance goal (PG; 21%). A one-sample Z-test will be used to test the one-sided hypothesis.

H_0: $P_{safety} \geq 21\%$

H_1: $P_{safety} < 21\%$

3.2.2 Statistical Methods

The primary analysis subset with sufficient 6-month follow-up will be eligible for inclusion in this endpoint analysis. The primary analysis subset with sufficient 6-month follow-up will be included in the denominator for the primary safety event rate. Subjects in the primary analysis subset with the occurrence of one of the following events between the time of implant and 6-month following the procedure will be included in the numerator for the primary safety event rate: all-cause mortality, all stroke, systemic embolism, and major bleeding.

A one-sample Z-test will be used to test the assumption that the composite rate of all-cause mortality, all stroke, systemic embolism, and major bleeding at 6 months ≥21%. The null hypothesis will be rejected if the resulting p-value is less than 0.025.

3.3 Primary Endpoint for Access System Subset

The primary endpoint for access system subset is the implant success rate, which is defined as implantation of a WATCHMAN FLX Pro device in the correct anatomical

position using the WATCHMAN TruSteer Access System. The implanted success rate will be evaluated by number of TruSteer Implant/number of subjects in the access system subset *100%. The analysis subsets are defined in 4.1.

The following hypothesis tests are based on the access system subset.

3.3.1 Hypotheses

A one-sample z-test will be used to test the null hypothesis that the implant success rate is less than PG:

H_0: $P_{TruSteer} \leq 94\%$
H_1: $P_{TruSteer} > 94\%$

3.3.2 Sample Size

The sample size was estimated based on the following assumptions:

- Expected rate for implant success in the access system subset ≥ 97.8% (based on historic studies of FLXibility, ICE LAA, WATCHMAN FLX-SURPASS, WATHCMAN FLX HK and PINNACLE FLX)
- Testing margin = 3.8%
- PG = 94% = expected rate (97.8%) - testing margin (3.8%)
- 1-sided significance level (α) = 0.025
- Power (1 minus ß) > 90%

Given the above assumptions, 300 subjects of access system subset will be required.

3.3.3 Statistical Methods

All enrolled subjects in the access system subset will be eligible for inclusion in this endpoint analysis. All enrolled subjects in the access system subset will be included in the denominator and access system subset with implant success will be included in the numerator.

A one-sample z-test will be used to test the null hypothesis that the implant success rate ≤94%. The null hypothesis will be rejected if the resulting p-value is less than 0.025.

4 GENERAL STATISTICAL METHODS

4.1 Subject Status and Classification

4.1.1 Screen Failure

A subject who signs an ICF but does not meet clinical eligibility criteria and/or is not treated or attempted to be treated with a WATCHMAN FLX Pro device is considered a screen failure. These subjects do not count towards the enrollment ceiling and will not be used for any planned endpoint analyses.

4.1.2 Attempt

A subject who signs an ICF, meets eligibility criteria, and has had a WATCHMAN Access Sheath inserted to implant the device, but does not receive a WATCHMAN FLX Pro device will be classified as "Attempt." Attempt subjects will be used for analyses of the ITT analyzed endpoints.

4.1.3 Implant

A subject who signs an ICF, meets eligibility criteria, and is implanted with the WATCHMAN FLX Pro device will be classified as "Implant." These subjects are followed in accordance with the follow-up schedule and included in all study analyses.

4.1.4 TruSteer Attempt

A subject who attempted with WATCHMAN TruSteer Access System but does not receive a WATCHMAN FLX Pro device with WATCHMAN TruSteer Access System will be classified as "TruSteer Attempt". Subjects who attempted with WATCHMAN TruSteer Access System but receives the device with other Access System will be also classified as "TruSteer Attempt". These subjects will be included in Access System Subset analyses.

4.1.5 TruSteer Implant

A subject who receives a WATCHMAN FLX Pro device with WATCHMAN TruSteer Access System will be classified as "TruSteer Implant". These subjects will be included in Access System Subset analyses.

4.2 Analysis Sets

Endpoints will be analyzed on an intention-to-treat (ITT) basis and an implanted basis. For ITT analyses, all subjects who sign the IEC-approved study ICF and are enrolled in the study will be included in the analysis, whether or not a study device was implanted. For implanted analyses, ITT subjects who had the study device implanted in the correct position during the index procedure will be included in the analysis.

- Primary analysis subset

The initial 500 patients enrolled in HEAL-LAA will be included in the primary analysis subset. Primary endpoints will be assessed on an intention-to-treat (ITT) basis and an implanted basis. The ITT analysis set includes all subjects who sign an Informed Consent Form, meet all clinical inclusion and no clinical exclusion criteria, and the WATCHMAN FLX Pro device has been used for treatment and/or attempted to be used for treatment. The hypothesis tests (PGs) are only based on the Primary Analysis Subset.

- Access system subset

The initial 300 TruSteer Attempt or TruSteer Implant subjects will be included in access system subset.

- Diversity Subset

Non-Caucasian subjects will be included in the diversity subset. There is no formal statistical hypothesis for this subset.

- Full enrollment set

All enrolled subjects will be included in this subset. There is no formal statistical hypothesis for this subset.

4.3 Control of Systematic Error/Bias

To control for the potential bias that could be introduced via sponsor classification of adverse events, an independent core laboratory will be used for analysis of certain endpoints at prespecified time points. A Clinical Events Committee (CEC) will adjudicate key endpoints and relevant adverse events.

4.4 Control of Type-I Error

For the primary analysis subset, due to the requirement that each applicable endpoint must be passed, each applicable endpoint can be tested at the significance level of 5% while still maintaining the overall type-I error level at no greater than 5%. This follows the methodology of the Intersection-Union Test (IUT). All study endpoints will be analyzed using one-sided significance levels of 2.5%.

4.4 Number of Subjects per Investigative Site

To avoid any site effect and bias, no site will be authorized to implant or attempt more than 15% of the primary analysis subset (first 500 enrolled subjects) (n = 75) without prior approval from the sponsor. Subjects exceeding this enrollment cap will be excluded from primary analysis set, but will still be retained in the full enrollment set. Sites that have reached the general enrollment cap may enroll additional subjects within the Diversity Subset. Enrollment cap waivers may be given for access system subset enrollment per the enrollment guide. To avoid any site effect and bias, no site will be authorized to implant or attempt more than 20% of the access system subset subjects (n = 60) without prior approval from the sponsor. . Subjects exceeding this enrollment cap will be excluded access analysis set, but will still be retained in the full enrollment set.

5 ADDITIONAL DATA ANALYSES

The additional data analysis in this section will be applied to all four analysis subsets: primary analysis subset, access system subset, diversity subset, and full enrollment set.

5.1 Other Endpoints/Measurements

No statistical hypothesis test will be conducted for other endpoints/measurements. The vairables of interest will be summarized using descriptive statistics for continuous variables (e.g., mean, standard deviation, n, minimum, maximum) and frequency tables or proportions for discrete variables. The Kaplan-Meier product-limit method will be used to estimate rates for time-to-event endpoints. Adverse event and serious adverse event (SAE) rates will be reported.

Additional endpoints will include the following:

1. CEC-adjudicated:
    - Device Success: Defined as implantation of a WATCHMAN FLX Pro device without in-hospital mortality.
    - All-cause mortality: Cardiovascular/unknown death and non-cardiovascular death
    - All Stroke: Disabling and non-disabling stroke; ischemic and hemorrhagic stroke
    - Bleeding: International Society on Thrombosis and Haemostasis (ISTH) major and non-major clinically significant
        - Procedural bleeding and non-procedural bleeding
    - Pericardial effusion/tamponade requiring pericardiocentesis or surgery
    - Systemic embolism

2. Site reported:
    - Device-related thrombus

5.2 Interim Analyses

There will be no formal interim analysis.

5.3 Subgroup Analyses

The following subgroups will be analyzed for the primary endpoints within the study:

- Sex (Female vs. Male)
- Age at time of consent (< 75 years vs. ≥ 75 years)
- Race/ethnicity
- Stroke risk (CHA_2DS_2-VASc Score)
- Bleeding risk (HAS-BLED Score)

5.4 Multivariable Analyses

Univariate and multivariate modeling analyses will be performed to assess the effect of baseline covariates on the primary effectiveness and safety endpoints. Logistic regression

will be used to assess the effects of possible predictors on the primary effectiveness and safety endpoints.

5.5 Other Analyses

Administrative analyses of safety data may be performed for regulatory agency review. Descriptive statistics of subject demographic, baseline characteristics, procedure characteristics, medical history will be presented for each analysis subset.
the overall study population

5.6 Changes to Planned Analyses

Any changes to the planned statistical analyses made prior to performing the analyses will be documented in an amended Statistical Analysis Plan approved prior to performing the analyses. Changes from the planned statistical methods after performing the analyses will be documented in the clinical study report along with a reason for the deviation.

6 VALIDATION

All clinical data reports generated per this plan will be validated per 90702587, Global WI: Clinical Data Reporting Validation.

7 PROGRAMMING CONSIDERATIONS

7.1 Format of Output

Results of analysis will be output programmatically to Microsoft Office® Word documents from SAS with no manual intervention. All output for the final statistical report will be in the form of a Word document containing tables, figures, graphs, and listings, as appropriate.

7.2 Methods for Handling Missing Data

All subjects who are enrolled will be eligible for evaluation, regardless of the treatment that ensues. Handling of dropouts and missing data will depend on their frequency and the nature of the outcome measure. Adjustments for missing outcomes data will be performed if deemed necessary to eliminate or minimize bias and will be described completely. Statistical models that account for censored data will be employed in appropriate circumstances, e.g., for time-to-event outcomes. Outlier values will be evaluated, and values determined to be invalid will be queried. All data will be included in the analysis unless judged to be invalid.

When calculating rates of adverse events for specific time intervals, missing and partial dates will be handled as shown below:

Partial Date Description	**Action Taken**
Entire onset date is missing	The implant procedure date will be used for

	the onset date.
The month and the day of the month are missing but the year is available	January 1st will be used for the month and day of the onset date. However, if the imputed date falls before the implant procedure date, then the implant procedure date will be used for the onset date.
Day is missing, but the month and year are available	The 1st will be used as the day of the onset date. However, if the imputed date falls before the implant procedure date, then the implant procedure date will be used for the onset date.

7.3 Rules and Definitions

Binary event rates (proportions) will be calculated on a per subject basis.

The number of subjects included in the safety endpoint outcome rates will be based on subjects who have adequate follow-up (see Section **Error! Reference source not found.**) and/or have experienced any CEC-confirmed events.

For baseline categorical variables, "unknown" responses and missing values will not be counted in rate denominators.

The date of last follow-up will be the latest of the following dates for each subject: site-reported adverse event date, CEC-confirmed event date, index procedure date, discharge date, follow-up visit date, and patient withdrawal (defined as: reasons = xx, xx, xx reasons) date from the end of study form.

Days to (event or last known status) = (event or status) date minus procedure date.

Note: subject withdrawal date should always be the last follow-up date and death date should be the subject last follow-up date if the subject didn't withdraw prior to death.

Length of hospital stay = discharge date minus procedure date.

In-hospital event rates are calculated as the proportion of subjects who experience the specified event from index procedure through day of discharge out of all subjects enrolled.

Out-of-hospital event rates are calculated as the proportion of subjects who experience the specified event from the day after discharge through the number of days as specified out of all subjects who were discharged following index procedure and have adequate follow-up or have experienced the event as specified.

7.4 CEC Binary Event Rates

The calculation method will follow the table below and extend to other endpoints and time points (e.g., 1-year death) with the appropriate modifications to the numbers of days. For example, for 90 days the event must have occurred within 90 days of procedure and the valid data point must be 60 days (early portion of window for the 90-day visit).

The following are the maximum days to event and number of days post-procedure that are adequate follow-up:

Follow-up Visit	Maximum Days to Event*	Days for Adequate Follow-up**
45 Days	45	30
6 Months	180	150
1 Year	365	335

*this is the target date for the follow-up visit except for the 1-year visit where this is the end of the visit window
**this is the start of the visit window

All event rates will be calculated relative to the date of index procedure (i.e., post-procedure).

7.5 Summarization of Site-Reported Serious and Non-Serious Adverse Events

Site-reported subject-based event rates will be calculated at various time points based on all events reported by the site. All enrolled subjects will be included in the analyses.

7.6 Medications

Missing and partial dates in medication start or stop date will be handled as shown in the table below.

Partial Date in start/stop date	**Action Taken**
Entire start date is missing	The procedure date will be used for the start date.
The month and the day of the month are missing but the year is available in start date	January 1st will be used for the month and day for start date.
Day is missing, but the month and year are available in start date	The 1st will be used as the start day.
Entire stop date is missing for discontinued medication	The start date will be used for the stop date.

Partial Date in start/stop date	Action Taken
The month and the day of the month are missing but the year is available in stop date	January 1st will be used for the month and day for stop date. However, if the imputed stop date falls before the start date, then the start date will be used for the stop date.
Day is missing, but the month and year are available in stop date	The 1st will be used as the stop day. However, if the imputed stop date falls before the start date, then the start date will be used for the stop date.

The following defined timeframe in medications.

Prior to implant: medication started prior to implant.
Post-implant: medication started and not stopped prior to implant OR medication started within 7 days post-implant.

14-day follow-up: medication started anytime (including prior to implant) up to 14 days and not stopped before 14 days post-implant.
45-day follow-up: medication started anytime (including prior to implant) up to 45 days and not stopped before 45 days post-implant.

3-month follow-up: medication started anytime (including prior to implant) up to 90 days and not stopped before 90 days post-implant.

1-year follow-up: medication started anytime (including prior to implant) up to 365 days and not stopped before 365 days post-implant.

8 BIBLIOGRAPHY

1. Post-Market Real World Outcomes in WATCHMAN FLX™ Pro Left Atrial Appendage Closure (LAAC) Device Protocol, 92986161 Rev/Ver B.