	Title:	Document No.
conformal® THE SHAPE OF STROKE PREVENTION	CONFORM Protocol Summary of Changes	C-15
	Version 9.0	

Study Name/Study Number:	CONFORM Pivotal/21-101
Protocol Revisions Being Captured	Rev L to M

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
Protocol Header; Title Page; Protocol Approval Page; Investigator Signature Page	Updated to reflect protocol Rev M and Revision date	Documentation control	N	N
Section 5 (schedule of assessments)-Footnotes 11 and 12	**Footnote 11** **From:** If a circumferential Pericardial Effusion measuring >10mm is detected on Cardiac CT, TTE evaluation is required for quantification **To:** If a Pericardial Effusion measuring >10mm is detected on Cardiac CT, TTE evaluation is required for quantification . **Footnote 12**	Safety consideration to require TTE evaluation and quantification of all types of pericardial effusions (not limited to circumferential effusions) observed on CT >10mm.	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	From: If TEE demonstrates a circumferential pericardial effusion measuring >10 mm, a TTE is required. **To:** If TEE demonstrates a pericardial effusion measuring >10 mm, a TTE is required.			
Protocol Synopsis and Section 8.6.2.2.2 Echocardiographic Exclusion Criteria	Echocardiographic Exclusion Criteria #4 **From:** Moderate or large pericardial effusion >10mm or symptomatic circumferential pericardial effusion, signs or symptoms of acute or chronic pericarditis, or evidence of tamponade physiology. **To:**	Removal of the word circumferential to exclude for any type of symptomatic pericardial effusion (not limited to circumferential pericardial effusion).	N	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Moderate or large pericardial effusion >10mm or symptomatic pericardial effusion, signs or symptoms of acute or chronic pericarditis, or evidence of tamponade physiology.			
Section 9.9-45-day Follow-up ± 7 Days (Telehealth Visit and Imaging) & Section 9.11 12-Month Follow-up ± 30 Days (Telehealth Visit and Imaging)	**From:** If a non-trivial circumferential Pericardial Effusion (defined as effusion measuring >10mm) is detected on Cardiac CT, TTE evaluation is suggested for quantification. **To:** If a non-trivial Pericardial Effusion (defined as effusion measuring >10mm) is detected on Cardiac CT, TTE evaluation is required for quantification.	Harmonization with section 5 of the protocol	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
Section 12.1-Reportable Events by Investigational Sites	**From:** • All adverse events of special interest. The following events, regardless of seriousness or relatedness, will be collected: o Bleeding events o Embolic events (e.g., stroke, TIA, systemic embolism) o Neurologic events o Device Embolizations o Device Related Thrombus **To:** • All adverse events of special interest. The following events, regardless of seriousness or relatedness will be collected: o Bleeding events o Embolic events (e.g., stroke, TIA, systemic embolism) o Neurologic events o Device Embolizations	Myocardial infarction, pericardial effusion, and vascular complications are reportable adverse events due to the cardiac nature. The list of Adverse Events of Special Interest was updated to specify events with additional data collection.	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	○ Device Related Thrombus ○ Myocardial Infarction ○ Pericardial Effusion ○ Vascular Complications			

Study Name/Study Number:	CONFORM Pivotal/21-101
Protocol Revisions Being Captured	Rev K to L (Not Released)

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
Protocol Header; Title Page; Protocol Approval Page; Investigator Signature Page; Study Contacts	1. Updated to reflect protocol Rev K and Revision date 2. Updated to change Conformal Clinical contact	1. Documentation control 2. New information	N	N
Investigational Sites-Protocol Synopsis	1. Revised # of sites in EU/EEA and Central Asia from 10 to 15	1. Allowance of 5 additional sites	N	N
Section 5 – Study Schedule of Assessments-Footnotes	**From:** [7] Neuro Assessment to include National Institute of Health Stroke Scale (NIHSS) and Modified Rankin Scale for Neurologic Disability (MRS) within 30 days of index procedure. **To:** [7]Neuro Assessment to include National Institute of Health Stroke Scale (NIHSS) and Modified Rankin Scale for Neurologic Disability (MRS) within 30 days of index procedure. The pre-discharge stroke	Edits for Clarifications	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	assessment must be done after the effects of anesthesia. **From:** [11] Cardiac CT may be used in lieu of TEE to screen for end point findings, e.g., DRT or >3mm Leak. • If a Device Related Thrombus is detected, a TEE is required to confirm the finding as soon as possible (recommended assessment within 2 weeks; at latest, 4-6 weeks from date of original study or at the patient's next follow up visit, whichever is first). • If a non-trivial leak is noted, a TEE is required to confirm the finding, as soon as possible (ideally within 2 weeks; at latest, 4-6 weeks from date of original study or at the patient's next follow up visit, whichever is first). *Note: A trivial leak is one in which filling is incomplete or is seen on*			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	only delayed imaging, with a gap that is ≤1mm. • If a non-trivial Pericardial Effusion (defined as circumferential effusion measuring >10mm) is detected on Cardiac CT, TTE evaluation is suggested for quantification. **To:** [11] Cardiac CT may be used in lieu of TEE to screen for end point findings, e.g., DRT or >3mm peri-device Leak. • If a Device Related Thrombus is detected, a TEE is required to confirm the finding as soon as possible (recommended assessment within 2 weeks; at latest, 4-6 weeks from date of original study or at the patient's next follow up visit, whichever is first). • If a non-trivial peri-device leak is noted on CT, a TEE is required to confirm the finding, as soon as possible (ideally within 2 weeks; at latest, 4-6 weeks from date of			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	original study or at the patient's next follow up visit, whichever is first). *Note: A non-trivial peri-device leak found on CT is one in which the site investigator determination indicates a likely finding of leak >3mm if measured by TEE.* • If a circumferential Pericardial Effusion measuring >10mm is detected on Cardiac CT, TTE evaluation is suggested for quantification. **From:** [12] TEE to include Apical 4 chamber (TTE) to assess for circumferential pericardial effusion. If TEE demonstrates a non-trivial pericardial effusion (defined as circumferential effusion measuring >10 mm, a TTE is required. **To:** [12] If TEE demonstrates a circumferential pericardial effusion measuring >10 mm, a TTE is required.			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Added: [16] INR levels required only for patients taking Warfarin, or in accordance with standard of care.			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
8.8.1 Roll-in population; 8.8.2 Conscious Sedation population; 8.8.3 Randomized population; 8.8.4 Implanted population; 8.8.5 Attempted Population	1. Revisions to analysis populations **8.8.1 Roll-In population** **From:** A Roll-In ITT subject is an individual who signs an ICF, is assigned to the Roll-In Cohort by the site and has an implant procedure attempted. For this population, an implant procedure attempt (ITT established) is defined when the LAAO Access Sheath is introduced into the body. Subjects who are scheduled for a roll-in procedure but no longer meet eligibility criteria and do not have a procedure attempt (i.e., the access sheath never entered the body) will be followed only through 45 days via telehealth/phone call visits (no imaging required and no protocol mandated medication therapy required). After the 45-Day visit, these subjects will have completed all required study assessments. **To:** A Roll-In ITT subject is an individual who signs an ICF, is assigned to the Roll-In Cohort by the site and has an implant procedure attempted. For this population, an implant procedure	1. Clarifying the follow up requirements for all subjects based on the analysis cohorts.	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	attempt (ITT established) is defined when the LAAO Access Sheath is introduced into the body. If an implant procedure is attempted without an implant placed, the subject must be followed through the Primary Safety and Efficacy Endpoints (at all visits including 7-days, 45-days, 6-months,12-months, and 18-months) assessing only: QVSFS, AE Assessment, and Concomitant Medication Assessment. These assessments can be conducted via telehealth/phone call. These subjects will not be required to have subsequent protocol mandated imaging and will not be required to follow the medication requirements. If a subject in the Roll-in population experiences a suspected stroke or systemic embolism, the subject should be brought in for an Unscheduled Visit (in-person clinic visit) for assessment per the Schedule of Assessments matrix. After the 18-Month visit, these subjects will have completed all required study assessments. Subjects who are scheduled for a roll-in procedure but no longer meet eligibility			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	criteria and do not have a procedure attempt (i.e., the access sheath never entered the body) will be followed only through 45 days via telehealth/phone call visits. No protocol mandated imaging or medication therapy will be required. After the 45-Day visit, these subjects will have completed all required study assessments and will be classified as Screen Failures. **8.8.2 Conscious Sedation Population** **From:** The Conscious Sedation ITT subject is an individual who signs an ICF, has been assigned to the Conscious Sedation Cohort and has an implant procedure attempted. For this population, an implant procedure attempt (ITT established) is defined when the CLAAS Delivery Catheter is introduced into the body. Subjects who are scheduled for a conscious sedation procedure but no longer meet			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	eligibility criteria and do not have a procedure attempt (i.e., the CLAAS Delivery Catheter never entered the body) will be followed only through 45 days via telehealth/phone call visits (no imaging required and no protocol mandated medication therapy required). After the 45-Day visit, these subjects will have completed all required study assessments. The Conscious Sedation ITT subject is an individual who signs an ICF, has been assigned to the Conscious Sedation Cohort and has an implant procedure attempted. For this population, an implant procedure attempt (ITT established) is defined when the CLAAS Delivery Catheter is introduced into the body. **To:** If an implant procedure is attempted without an implant placed, the subject must be followed through the Primary Safety and Efficacy Endpoints (at all visits including 7-days, 45-days, 6-months,12-months, and 18-months) assessing only: QVSFS, AE Assessment, and Concomitant Medication Assessment. These assessments can be conducted via telehealth/phone call. These			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	subjects will not be required to have subsequent protocol mandated imaging and will not be required to follow the medication requirements. If a subject in the Conscious Sedation Population experiences a suspected stroke or systemic embolism, that subject should be brought in for an Unscheduled Visit (in-person clinic visit) for assessment per the Schedule of the Assessments matrix. After the 18-Month visit, these subjects will have completed all required study assessments. Subjects who are scheduled for a conscious sedation procedure and no longer meet eligibility criteria and do not have a procedure attempt (i.e., the CLAAS Delivery Catheter never entered the body) will be followed only through 45 days via telehealth/phone call visits. No protocol mandated imaging or medication therapy will be required. After the 45-Day visit, these subjects will have completed all required study assessments and will be classified as Screen Failures. **8.8.3 Randomized Population** **From:**			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	A Randomized subject is an individual who signs ICF and is found to meet all eligibility criteria and is randomized. When a subject is randomized, he/she will be included in the Intention to Treat population. The Randomized Population includes two groups: 1) subjects who undergo LAAO Procedure and 2) subjects who after randomization and prior to the study procedure are found to no longer meet eligibility criteria. Examples include subjects after randomization while awaiting the procedure fall and sustain a fractured hip. Also included are subjects who are brought to the Cardiac Catheterization Laboratory who on baseline TEE evaluation are found to have thrombus in the LAA. Subjects who are randomized, no longer meet eligibility criteria, and do not have a procedure attempt (i.e., the access sheath never entered the body) will be followed only through 45 days via telehealth/phone call visits (no imaging required and no protocol mandated medication therapy required). After			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	the 45-Day visit, these subjects will have completed all required study assessments. **To:** A Randomized subject is an individual who signs ICF and is found to meet all eligibility criteria and is randomized. When a subject is randomized, he/she will be included in the Intention to Treat population. The Randomized Population includes two groups: 1) subjects who undergo LAAO Procedure and 2) subjects who after randomization and prior to the study procedure are found to no longer meet eligibility criteria. Examples include subjects after randomization while awaiting the procedure fall and sustain a fractured hip. Also included are subjects who are brought to the Cardiac Catheterization Laboratory who on baseline TEE evaluation are found to have thrombus in the LAA. Subjects who are randomized and no longer meet eligibility criteria (group 2 above) must be followed through the Primary Safety and Efficacy Endpoints with telehealth/phone call			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	visits (at all visits including 7-days, 45-days, 6-months, 12-months, and 18-months) assessing only: QVSFS, AE Assessment, and Concomitant Medication Assessment. These subjects will not be required to have subsequent protocol mandated imaging and will not be required to follow the medication requirements. If a subject in the Randomized Population group experiences a suspected stroke or systemic embolism, that subject should be brought in for an Unscheduled Visit (in-person clinic visit) for assessment per the Schedule of Assessments matrix. After the 18-Month visit, these subjects will have completed all required study assessments. **8.8.4 Attempted Population** **From:** The Attempted Population includes all ITT subjects in whom a LAAO procedure has been attempted, i.e., the LAAO access sheath was inserted into the body. The Attempted Population includes two groups: 1) subjects who undergo LAAO Procedure and receive a LAAO Closure Device and 2) subjects in whom a undergo the			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	procedure without a LAAO device being placed. These subjects in the Attempted Population who did NOT receive an implant will not be required to have subsequent protocol mandated LAA imaging and will not be required to follow the device medication requirements. Subjects who do not receive an implant must be followed through the Primary Safety and Efficacy Endpoints with telehealth/phone call visits (at all visits including 7-days, 45-days, 6-months, 12-months, and 18-months) assessing only: QVSFS, AE Assessment, and Concomitant Medication Assessment. If a subject in the Attempted Population group experiences a suspected stroke or systemic embolism, that subject should be brought in for an Unscheduled Visit (in-person clinic visit) for assessment per the Schedule of Assessments matrix. After the 18-Month visit, these subjects will have completed all required study assessments. **To:**			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	The Attempted Population includes all ITT subjects in whom a LAAO procedure has been attempted, i.e., the LAAO access sheath was inserted into the body. The Attempted Population includes two groups: 1) subjects who undergo LAAO Procedure and receive a LAAO Closure Device and 2) subjects in whom a undergo the procedure without receiving a LAAO device. Following index procedure hospitalization discharge, these subjects in the Attempted Population who do NOT receive an implant will not be required to have subsequent protocol mandated imaging and will not be required to follow the medication requirements. Subjects who do not receive an implant must be followed through the Primary Safety and Efficacy Endpoints with telehealth/phone call visits (at all visits including 7-days, 45-days, 6-months, 12-months, and 18-months) assessing only: QVSFS, AE Assessment, and Concomitant Medication Assessment. If a subject in the Attempted Population group experiences a suspected stroke or systemic embolism, that subject should be brought in for an			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Unscheduled Visit (in-person clinic visit) for assessment per the Schedule of Assessments matrix. After the 18-Month visit, these subjects will have completed all required study assessments. **8.8.5 Implanted Population** **From:** The Implanted Population includes all subjects in the Attempted Population who undergo the study procedure and receive a LAAO device. Please note that this includes subjects who have received the assigned device or an alternative commercially available device. For subjects assigned to the CLAAS Cohort, the assigned device is the CLAAS Device. For subjects assigned to the Control Cohort, the assigned device will be the first device introduced into the body. These subjects are followed in accordance with the follow-up schedule. All applicable case report forms per the protocol must be completed.			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	To: The Implanted Population includes all subjects in the Attempted Population who undergo the study procedure and receive a LAAO device. Please note that this includes subjects who have received the assigned device or an alternative commercially available device. For subjects assigned to the CLAAS Cohort, the assigned device is the CLAAS Device. For subjects assigned to the Control Cohort, the assigned device will be the first device introduced into the body. If at any point, a patient was implanted with a LAAO device and has that implant removed, the patient must be followed through the Primary Safety and Efficacy Endpoints with telehealth/phone call visits (at all visits including 7-days, 45-days, 6-months, 12-months, and 18-months) assessing only: QVSFS, AE Assessment, and Concomitant Medication Assessment. These subjects will not be required to have subsequent protocol mandated imaging and will not be required to follow the medication requirements.			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	These subjects are followed in accordance with the follow-up schedule.			
8.9.1 Withdrawal	**1. Added:** The Study Exit form shall be completed in the EDC documenting the patient's Withdrawal status.	1. Edit for clarification	N	N
8.10 Lost to Follow-up	**From:** When a subject does not return for a clinic visit or is not reachable by telephone or other contact, this event is considered a missed visit. Subjects with a missed visit may return for subsequent follow-up visits. If a subject has a missed visit and has not withdrawn from the trial, site personnel should make all reasonable efforts to locate and communicate with the subject, including the following: A minimum of (3) three telephone calls to contact the subject should be recorded in the	Clarification on amount of missed visits for LTFU designation	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	source documentation, including date, time, and initials of site personnel trying to make contact. If these phone calls are unsuccessful, a letter should be sent to the subject to document lack of responsiveness to confirm the lost to follow-up status. **To:** When a subject does not return for a clinic visit or is not reachable by telephone or other contact, this event is considered a missed visit. Subjects with a missed visit may return for subsequent follow-up visits. If a subject has a missed visit and has not withdrawn from the trial, site personnel shall make all reasonable efforts to locate and communicate with the subject. Specifically, a minimum of (3) three telephone calls per missed visit to contact the subject shall be recorded in the source documentation, including date, time, and initials of site personnel trying to make contact. Subjects who miss four consecutive visits shall be considered Lost to Follow-up. The Study Exit form shall be completed in the EDC			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	documenting the patient's Lost to Follow-up status. If a subject becomes Lost to Follow-up, a letter shall be sent to the subject to document lack of responsiveness to confirm the Lost to Follow-up status.			
9.2 Screening/Baseline Imaging	1. Added: A TEE or CT older than 6 months may be used to evaluate anatomic selection criteria (and cannot be used to evaluate for LV function, pericardial effusion).	1. Allowance of TEE or CT older than 6 months to be used to evaluate anatomic selection criteria as subjects are re-evaluated during procedural TEE	N	N
9.3 Pre-Procedural Review	1. Updated to note historical imaging can be performed within 6 months of consent	1. Edits for clarification	N	N
9.6.2 Additional Considerations	**From:** **Inadequate seal**: Subjects with inadequate seal (residual leak >5mm) at the post-deployment TEE (or any subsequent TEE or Cardiac CT) should be evaluated for treatment with DOAC and ASA for 4-6 weeks followed by repeat TEE. If inadequate seal persists on TEE, antithrombotic therapy should be considered until seal is confirmed on follow up imaging. Antithrombotic therapy should be individualized to the subject based on	Clarified repeat imaging and core-lab requirement review as follows: Repeat imaging should be conducted per SOC. Resolution of inadequate seal must be documented on follow up imaging. All additional SOC imaging (TEE or Cardiac CT) should be provided to the Sponsor for Core Lab Review	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	anatomic (size of leak) and clinical (risk of anticoagulation) considerations. **Device Related Thrombus**: If thrombus is detected on the LA surface of the device on the post-procedure TEE (or any subsequent TEE or Cardiac CT), the subject should be evaluated for treatment with OAC (Warfarin or DOAC), and ASA for 4-6 weeks followed by repeat imaging. Antithrombotic therapy should be continued until confirmation of thrombus resolution has been documented on follow up imaging. Antithrombotic therapy should be individualized to the subject based on clinical (risk of anticoagulation) considerations. **To:** **Inadequate seal**: Subjects with inadequate seal (residual leak >5mm) at the post-deployment TEE (or any subsequent TEE or Cardiac CT) should be evaluated for treatment with DOAC and ASA for 4-6 weeks followed by repeat TEE. If inadequate seal persists on TEE, antithrombotic therapy should be considered until seal is confirmed on follow up imaging. Repeat imaging should be conducted per SOC.			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Resolution of inadequate seal must be documented on follow up imaging. All additional SOC imaging (TEE or Cardiac CT) should be provided to the Sponsor for Core Lab Review. Antithrombotic therapy should be individualized to the subject based on anatomic (size of leak) and clinical (risk of anticoagulation) considerations. **Device Related Thrombus:** If thrombus is detected on the LA surface of the device on the post-procedure TEE (or any subsequent TEE or Cardiac CT), the subject should be evaluated for treatment with OAC (Warfarin or DOAC), and ASA for 4-6 weeks followed by repeat imaging. Repeat imaging should be conducted per SOC or at the patient's next study visit. All additional SOC imaging (TEE or Cardiac CT) should be provided to the Sponsor for Core Lab Review. Antithrombotic therapy should be continued until confirmation of thrombus resolution has been documented on follow up imaging. Antithrombotic therapy should be individualized to the subject based on clinical (risk of anticoagulation) considerations.			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
9.14 Suspected Stroke or Systemic Embolism Neurologic Events (Unscheduled Visit)	**1. Added:** • In the event of a Stroke, 90 days following the event, documentation of a Neurologic evaluation including Modified Rankin Scale (mRS) is required. The Sponsor may request records (including imaging) related to this evaluation. • In the event of a Systemic Embolism, 90 days following the event, documentation of a clinical evaluation is required. The Sponsor may request records (including imaging) related to this evaluation.	1: Added requirements/evaluation 90 post-stroke or systemic embolism	N	N
12 Safety Reporting	**1. Added:** Adverse event collection for the study will occur from the time of randomization in the RCT cohort and at the time of consent for the Roll-In Cohort and Conscious Sedation Sub-study Cohort.	1. Edits for clarification regarding timing of AE collection for Roll-in and conscious sedation sub-study cohorts	N	N
12.3 Device Deficiencies	1. Added data collection for device deficiencies for control devices (comparator devices)	1. Allows for comparison of device deficiencies between CLASS and Control devices	N	N
16.2 Source Documentation	1. Added additional source documents to be collected:	1. Enhances adjudication of safety events	N	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	• In the event of subject death, Conformal may request a detailed statement (death letter) providing circumstances around the death signed and dated by the investigator. • Death certificate, if available • Autopsy report, if available			
21.1 Appendix A: Definitions	**1. Added to Bleeding Event definition:** All bleeding events (regardless of BARC classification) should be reported	1. Edit for clarification	N	N

Minor administrative/clerical changes related to formatting and consistency in terminology throughout the protocol were made.

Study Name/Study Number:	CONFORM Pivotal/21-101
Protocol Revisions Being Captured	Rev J.1 to K

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
Section 5 – Study Schedule of Assessments-Footnote 10	**From:** [10] Implanted subjects only (does not include patients who did not receive a LAAO device). TTE is required to surveil for pericardial effusion. The study must be performed a minimum of 3 hours after discharge from cardiac catheterization laboratory. **To:** [10] Implanted subjects only (does not include patients who did not receive a LAAO device). TTE is required to surveil for pericardial effusion. The study must be performed at a minimum of 4 hours from the end of the procedure (removal of the access sheath) . Schedule of assessment table was also revised from 3 to 4 hours for discharge.	Safety Considerations	Y	Y
Section 9.7 Pre-Discharge Follow-Up	**From:**	Safety Considerations	Y	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Subjects are required to stay in the hospital a minimum of 3 hours post-procedure. Post-procedure assessment must occur during the index procedure hospitalization prior to hospital discharge or at 7 days post index procedure, whichever is sooner. The evaluation must include: • TTE is required to surveil for pericardial effusion. The study must be performed a minimum of 3 hours after discharge from the cardiac catheterization laboratory. **To:** Subjects are required to stay in the hospital a minimum of 4 hours post-procedure. Post-procedure assessment must occur during the index procedure hospitalization prior to hospital discharge or at 7 days post index procedure, whichever is sooner. The evaluation must include: • TTE is required to surveil for pericardial effusion. The study must be performed at a minimum of 4 hours from the end of the procedure (removal of the access sheath).			

Study Name/Study Number:	CONFORM Pivotal/21-101
Protocol Revisions Being Captured	Rev E to J.1

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
Protocol Header; Title Page; Protocol Approval Page; Investigator Signature Page; Study Contacts	3. Updated to reflect protocol Rev J.1 and Revision date 4. Updated to change Conformal Clinical contact	3. Documentation control 4. New information	N	N
Title Page 4 Protocol Synopsis	1. Added separate and unique NCT Number for Conscious Sedation Sub-Study	1. Added per CMS request following Protocol Rev C.	N	N
1 Acronyms	1. Added Transseptal Puncture Access (TSP) to list of acronyms 2. Added EU/EEA (European Union/European Economic Area)	1. Consistency with protocol	N	N
3 Study Contacts	1. Updated Conformal Clinical contact 2. Added Authorized Representative for Conformal Medical in European Union: FGK Representative Service Ireland, Ltd	1. New information 2. EU MDR requirement in alignment with ISO 14155:2020	N	N
4 Protocol Synopsis; 6.2 Current Standard of Care to Treat Atrial Fibrillation; 6.3 Conformal Prague Study; 6.4 US Early Feasibility IDE	1. Updated references from “Conformal” or “CLAAS Device” to “CLAAS”, “CLAAS System”, “CLAAS Implant” where applicable	1. Consistency with Instructions for Use	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
Clinical Study; 7.4.1 Overview; 7.4.1.3 Delivery System; 8.1 Study Objectives; 8.2 Study Design and Rationale; 8.3 Number of Required Subjects; 8.4 Estimated Enrollment Time; 8.6.2.2.2 Echocardiographic Exclusion Criteria; 9.2 Screening/Baseline Imaging; 9.5 Index Procedure; 12.7 Expected Adverse Events – Risk/Benefit Analysis; 12.4 Unanticipated Adverse Device Effects; 12.8 Methods to Minimize Risks; 12.9 Potential Benefits; 12.10 Benefit-Risk Assessment; 17 Device Accountability; 19.2.1 Specific Investigator Training Requirements; 21.9 Appendix E: Conscious Sedation Sub-Study Protocol				
4 Protocol Synopsis; 8.2 Study Design and Rationale; 8.3 Number of Required Subjects	1. Added separate and unique NCT Number for Conscious Sedation Sub-Study	1. Edits for consistency	N	N
4 Protocol Synopsis	From: 1. Roll-in Phase**:** a maximum of three subjects per site can be enrolled as roll-in cases for a maximum of 300 subjects. To:	1. A maximum of 300 Roll-in subjects study wide is permissible per FDA	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	1. Roll-in Phase: a maximum of 300 subjects can be enrolled as roll-in cases.			
4 Protocol Synopsis; 8.6.2.2.1 General Exclusion Criteria	1. Updated General Exclusion Criteria #2 from "procedure (e.g., prior atrial septal defect [ASD] or high-risk patent foramen ovale [PFO] surgical repair or implanted closure device, or obliterated or ligated left atrial appendage)." to "e.g., atrial septal defect (ASD) requiring closure, high-risk patent foramen ovale (PFO) requiring closure, a highly mobile inter-atrial septal aneurysm precluding a safe TSP, presence of a PFO/ASD closure device, history of surgical ASD repair or history of surgical LAAO closure." 2. Updated General Exclusion Criteria #4 and #13 to specify "prosthetic" mechanical heart valve. 3. Exclusion Criteria #8: added "major" Recent (**within 30 days** of index procedure) or planned (**within 60 days** post-procedure) cardiac or major non-cardiac	1. Edits for clarification 2. Edits for clarification 3. Edit for clarification	N	Y
4 Protocol Synopsis; 8.6.2.2.2 Echocardiographic Exclusion Criteria	1. Updated Echocardiographic Exclusion Criteria 1 from "CLAAS device" to "CLAAS Implant" and specified devices apply to	1. Consistency with Instructions for Use; Edits for clarification	N	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	both the investigational device "CLAAS" and a commercially available device.			
4 Synopsis; 8.6.2.1.1 General Inclusion Criteria	1. Removed CHADS2 from eligibility criteria	1. CHADS2 has been superseded by the CHA_2DS_2Vasc score as the standard clinical instrument to assess AF associated stroke.	N	Y
4 Protocol Synopsis; 9.1.6 Post-Procedure; 21.9 Appendix E: Conscious Sedation Sub-Study Protocol	1. Re-added footnote from prior versions where "Clopidogrel*" is noted: NOTE: A substitute P2Y12 inhibitor (i.e., prasugrel, ticagrelor) may be used as per managing physician's judgement. For patients who are known clopidogrel non-responder an alternative P2Y12 inhibitor should be used.	1. Edits for clarification	N	N
5 Study Schedule of Assessments	1. Added respective days to 6 months and 1-year follow-up visits 2. Removed vital signs at pre-discharge and 18 months 3. Revised footnote #9 to reflect imaging requirements at screening **From:** **<u>Screening imaging must be performed prior to randomization.</u>** In sites without the appropriate CLAAS experience, Pre-Procedural Imaging Review supported by TEE or CT performed within 6 months prior to consent is required for the initial 5 subjects scheduled	1. Edit for clarification 2. Vital signs are not required per standard of care 3. Edits for clarification	Y	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	for implant. For subsequent patients, TTE, TEE, Cardiac CT OR MRI performed within 6 months prior to consent may be used to assess the Echo Exclusion Criteria. TTE or MRI may be used to assess some Echo Exclusion Criteria as applicable, however, neither TTE or MRI can be utilized as the sole imaging modality to assess the Echo Exclusion Criteria. If no historical imaging is available, imaging must be performed prior to randomization. If a significant cardiac event occurs after the cardiac imaging which causes a change in cardiac status [i.e., major Congestive Heart Failure (CHF) decompensation] the screening imaging must be repeated after informed consent and prior to randomization. **To:** **Screening imaging (TEE or CT) must be performed prior to randomization.** Imaging is required to assess the anatomic screening criteria. Cardiac CT or TEE can be used to assess all Echocardiographic Eligibility Criteria. TTE and MRI studies are limited to the assessment of Left ventricular ejection fraction and for detection of pericardial effusions. TTE and MRI cannot be used to			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	assess other Echocardiographic Eligibility Criteria. 4. Revised footnote #11 to reflect imagining requirements for endpoint analyses **From:** Cardiac CT may be used in lieu of TEE. If a finding of Pericardial Effusion, Device Related Thrombus or inadequate seal is detected on Cardiac CT, a TEE is required to confirm finding **To:** Cardiac CT may be used in lieu of TEE to screen for end point findings, e.g., DRT or >3mm Leak. 1. If a Device Related Thrombus is detected, a TEE is required to confirm the finding as soon as possible (recommended assessment within 2 weeks; at latest, 4-6 weeks from date of original study or at the patient's next follow up visit, whichever is first). • If a non-trivial leak is noted, a TEE is required to confirm the finding, as soon as possible (ideally within 2 weeks; at	4. Edits for clarification; Safety considerations		

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	latest, 4-6 weeks from date of original study or at the patient's next follow up visit, whichever is first). *Note: A trivial leak is one in which filling is incomplete or is seen on only delayed imaging, with a gap that is ≤1mm.* • If a non-trivial Pericardial Effusion (defined as circumferential effusion measuring >10mm) is detected on Cardiac CT, TTE evaluation is suggested for quantification. 5. Added CBC in alignment with Inclusion/Exclusion Criteria 6. Consolidated references from "EKG" and "ECG" to "ECG" 7. Updated TTE footnote 8. Updated Brain Imaging footnote(s) 9. Updated Medication Review footnote 10. Revised randomization timing	5. Edits for clarification 6. Edits for clarification 7. Edits for clarification 8. Edits for clarification 9. Edits for clarification 10. Edits for clarification		
5 Study Schedule of Assessments; 9.1 Screening/Baseline	1. Included Cardiac CT as option to be performed at Screening, 45-day, and 12 Month visits and updated footnote(s) in	1. Safety considerations	Y	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Schedule of Assessments table; Updated description in Screening/Baseline section 9.1			
5 Study Schedule of Assessments; 9.1 Screening/Baseline; 9.12 Eighteen-month Follow-up ± 30 Days (Clinic Visit); 9.14 Suspected Stroke or Systemic Embolism Neurologic Events (Unscheduled Visit); 19.2 Training of Investigators and Research Staff	1. Updated description for Neuro Assessments in applicable sections	1. Edits for clarification/allow for flexibility for performing assessments per standard of care	N	N
5 Study Schedule of Assessments; 9.1 Screening/Baseline; 9.14 Suspected Stroke or Systemic Embolism Neurologic Events (Unscheduled Visit)	1. Consolidated references from "Physical Exam" and "Physical Assessment" to "Physical Exam/Assessment".	1. Edits for clarification	Y	Y
5 Study Schedule of Assessments; 9.5 Index Procedure	1. Updated TEE footnote(s) in Schedule of Assessments table and updated description in Index Procedure section	1. Edits for clarification	N	N
6 Introduction	1. Added “Conformal is a privately held medical device company which is providing funding for this clinical investigation.”	1. EU MDR requirement in alignment with ISO 14155:2020	N	N
7.4.1 Overview 7.4.1.3 Delivery System	1. Makeup of CLAAS delivery System: Removed Hydraulic Loader	1. The optional Hydraulic Loader is being removed from the portfolio of CLAAS products. This accessory will no longer be available.	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
7.4.1.3 Delivery System	Added language regarding the optional use of VizaraMed Multiflex Steerable Sheath: 1. The VizaraMed Multiflex Steerable Sheath 15.5F has been evaluated for compatibility with the Regular (27 mm) CLAAS System and may be used as an alternative to the Regular Conformal Access Sheath. The 15.5F VizaraMed Multiflex Steerable Sheath is not compatible with the Large (35 mm) CLAAS System.	1. Consistency with Instructions for Use	N	N
7.4.1.4 Device Traceability	1. Added section Device Traceability	1. EU MDR requirement in alignment with ISO 14155:2020	N	N
7.4.1.1 Initial CLAAS and Next Generation CLAAS Systems	1. Added description of changes from initial CLAAS systems utilized from June 2022-April 2024 and next generation CLAAS Systems 2. Updated Figures 3-5 to reflect next generation CLASS Systems 3. Updated working length of delivery Catheter Table 2	1. Consistency with Instructions for Use 2. Consistency with Instructions for Use 3. Consistency with Instructions for Use	N	N
7.4.1.5 Control Devices	1. Updated from 3 to 4 FDA approved LAAO devices	1. Edit for clarification	N	N
8 Study Design; Table 1: CONFORM Milestones and Timeline	1. Updated to reflect current milestones and timelines	1. Revised to reflect current milestones and timelines	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
8.1.6 Informed Consent	1. Added references to EC (Ethics Committee)	1. EU MDR requirement in alignment with ISO 14155:2020.	N	N
8.2.1 Roll-In Phase; 8.3.1 Roll-in Phase	1. Updated to up to 300 subjects study-wide may be implanted with the CLAAS Implant as roll-in cases. Investigational sites that implanted 3 subjects with the Initial CLAAS system will be permitted to implant one additional subject with the Next Generation CLASS System. Additional investigational sites will be permitted to implant up to a maximum of 3 roll-in subjects (Initial CLAAS System and Next Generation CLAAS System combined	1. To ensure adequate implant experience with the next generation CLAAS Systems	Y	N
8 Study Design; Table 2: CONFORM Milestones and Timeline	1. Updated to reflect current milestones and timelines	1. Revised to reflect current milestones and timelines	N	N
8.7 Informed Consent	1. Updated reference from ISO 14155 to ISO 14155:2020	1. Edit for clarification	N	N
16.1 Data Collection and Monitoring	Added: "The EDC system will meet applicable requirements as set forth by FDA or other regulatory authorities. An audit trail will be available for tracking all data that the EDC user enters, modifies or deletes.	1. EU MDR requirement in alignment with ISO 14155:2020	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	The data entered the EDC will be fully validated as described in the Data Management Plan and/or related documents, which may include using clinical investigation-specific range and consistency checks and database listings. Queries may be issued to the site via the EDC system and resolved by the investigator or his/her designee using the EDC. Data validation will be completed on a regular basis. The entire database will be re-validated to ensure that there are no outstanding data discrepancies prior to database lock. Any changes to the database after that time will require written agreement by the Sponsor."			
8.8.1 Roll-in population; 8.8.2 Conscious Sedation population; 8.8.3 Randomized population; 8.8.4 Implanted population; 8.8.5 Attempted Population	1. Revisions to analysis populations **From:** **8.7.2 ITT Randomized Population** A randomized subject is an individual who signs informed consent and is randomized. This group of subjects is included in the Intention to Treat population. The ITT subjects will be used to evaluate the Primary Efficacy and Primary Safety Endpoints. All other study populations are considered secondary and supportive in nature.	1. Clarifying the follow up requirements for all subjects based on the analysis cohorts.	Y	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	8.7.3 Time of Enrollment Definitions: RCT Group ITT: includes all randomized subjects that sign an informed consent form. Roll-In Cohort ITT: includes all subjects that sign an informed consent form and have an implant procedure attempt. Conscious Sedation ITT: includes all subjects that sign an informed consent form and have an implant procedure scheduled. **8.7.3 Intended Population** A Randomized subject that does not have an implant attempt (i.e., a LAAO Access Sheath is never inserted into the body) will be classified as an "Intent" subject. These subjects will be monitored for safety through 45 days post procedure and will then be exited from the study. These subjects will not be required to have any LAA imaging and will not be required to follow the device medication requirements. **8.7.4 Attempted Population** A subject that has a LAAO Access Sheath inserted into the body to implant the device, but eventually does not receive a Device will be classified as "Attempt." Attempt subjects count towards the enrollment ceiling and will be used for analyses of the endpoints			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	according to intention to- treat principles. These subjects will be monitored for safety through 45 days post procedure and will then be exited from the study. These subjects will not be required to have any LAA imaging and will not be required to follow the device medication requirements. Any prescribed antiplatelet, aspirin, and anticoagulant medications must be captured in the medication logs through the final 45 day follow up visit for completeness. All applicable case report forms per the protocol must be completed. The original signed informed consent and any relevant documentation must be maintained in the site's subject file. **8.7.5 Implanted Population** A subject who is successfully implanted with a Device will be classified as an "Implant." Successfully implanted subjects are those defined as having technical success, where the device has been deployed and implanted in the correct position. These subjects are followed in accordance with the follow-up schedule. All applicable case report forms per the protocol must be completed. The original			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	signed informed consent and any relevant documentation must be maintained in the site's subject file. **To:** **8.8.1 Roll-In Population** A Roll-In ITT subject is an individual who signs an ICF, is assigned to the Roll-In Cohort by the site and has an implant procedure attempted. For this population, an implant procedure attempt (ITT established) is defined when the LAAO Access Sheath is introduced into the body. Subjects who are scheduled for a roll-in procedure, but no longer meet eligibility criteria and do not have a procedure attempt (i.e., the access sheath never entered the body) will be followed only through 45 days via telehealth/phone call visits (no imaging required and no protocol mandated medication therapy required). After the 45-Day visit, these subjects will have completed all required study assessments. **8.8.2 Conscious Sedation Population**			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	The Conscious Sedation ITT subject is an individual who signs an ICF, has been assigned to the Conscious Sedation Cohort and has attempted an implant procedure. For this population, an implant procedure attempt (ITT established) is defined when the CLAAS Delivery Catheter is introduced into the body. Subjects who are scheduled for a conscious sedation procedure, but no longer meet eligibility criteria and do not have a procedure attempt (i.e., the CLAAS Delivery Catheter never entered the body) will be followed only through 45 days via telehealth/phone call visits (no imaging required and no protocol mandated medication therapy required). After the 45-Day visit, these subjects will have completed all required study assessments. **8.8.3 Randomized Population** A Randomized subject is an individual who signs ICF and is found to meet all eligibility criteria and is randomized. When a subject is randomized, he/she will be included in the Intention to Treat population. The Randomized Population includes two groups: 1) subjects who undergo LAAO Procedure and 2) subjects who after			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	randomization and prior to the study procedure are found to no longer meet eligibility criteria. Examples include subjects after randomization while awaiting the procedure fall and sustain a fractured hip. Also included are subjects who are brought to the Cardiac Catheterization Laboratory who on baseline TEE evaluation are found to have thrombus in the LAA. Subjects who are randomized no longer meet eligibility criteria, and do not have a procedure attempt (i.e., the access sheath never entered the body) will be followed only through 45 days via telehealth/phone call visits (no imaging required and no protocol mandated medication therapy required). After the 45-Day visit, these subjects will have completed all required study assessments. **8.8.4 Attempted Population** The Attempted Population includes all ITT subjects in whom a LAAO procedure has been attempted, i.e., the LAAO access sheath was inserted into the body.			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	The Attempted Population includes two groups: 1) subjects who undergo LAAO Procedure and receive a LAAO Closure Device and 2) subjects in whom a undergo the procedure without a LAAO device being placed. These subjects in the Attempted Population who did NOT receive an implant will not be required to have subsequent protocol mandated LAA imaging and will not be required to follow the device medication requirements. Subjects who do not receive an implant must be followed through the Primary Safety and Efficacy Endpoints with telehealth/phone call visits (at all visits including 7-days, 45-days, 6-months, 12-months, and 18-months) assessing only: QVSFS, AE Assessment, and Concomitant Medication Assessment. If a subject in the Attempted Population group experiences a suspected stroke or systemic embolism, that subject should be brought in for an Unscheduled Visit (in-person clinic visit) for assessment per the Schedule of Assessments matrix. After the 18-Month visit, these			

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	subjects will have completed all required study assessments. **8.8.5 Implanted Population** The Implanted Population includes all subjects in the Attempted Population who undergo the study procedure and receive a LAAO device. Please note that this includes subjects who have received the assigned device or an alternative commercially available device. For subjects assigned to the CLAAS Cohort, the assigned device is the CLAAS Device. For subjects assigned to the Control Cohort, the assigned device will be the first device introduced into the body. These subjects are followed in accordance with the follow-up schedule. All applicable case report forms per the protocol must be completed.			
8.9.1 Withdrawal	1. Updated section from "Voluntary Withdrawal" to "Withdrawal) 2. Added: Subjects who withdraw/are withdrawn from the study should undergo follow-up-treatment and care according to the	1. EU MDR requirement in alignment with ISO 14155:2020 2. EU MDR requirement in alignment with ISO 14155:2020	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	institutional standards of care provided by the physicians for patients undergoing left atrial appendage closure. Subjects who withdraw from the study will not be replaced.			
8.10 Loss to Follow-up 8.11 Study Completion	2. Revised from "voluntary withdraw(n)" to "withdraw(n)"	2. EU MDR requirement in alignment with ISO 14155:2020	N	N
8.11 Study Completion	1. Added: Subjects who complete the study (i.e., complete final protocol-specified follow-up assessment) should undergo follow-up treatment and care according to the institutional standards of care provided by the physicians for patients undergoing left atrial appendage closure.	1. EU MDR requirement in alignment with ISO 14155:2020	N	N
9.1 Screening/Baseline	2. Updated assessment of neurological assessment • Not required for randomization 3. An additional platelet count, HCT/HgB lab testing must be collected within 48 hours prior to the index procedure.	2. Edit for clarification 3. Moved to section 9.5-Index procedure	N	N
9.1.1 Screening/Baseline; 14.4 Baseline Characteristics	1. Clarified medical and surgical history includes NYHA and anginal status (may be done per standard of care up to 30 days prior to consent).	1. Edits for clarification	N	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
9.1.1 Screening/Baseline; 9.7 Pre-discharge Follow-up; 9.12 Eighteen-month Follow-up ± 30 Days (Clinic Visit)	1. Updated Vital Signs footnote in Schedule of Assessments table and updated description in Screening/Baseline. Vital Signs may be collected up to 60 days prior to consent. Height to be collected at Screening Visit only (not pre-discharge and 18-Month Follow-up). Weight to be collected at Screening Visit and 18-Month Follow-up (not pre-discharge)	1. Edits for clarification. Height not expected to change over course of study.	Y	Y
9.2 Screening/Baseline Imaging	1. Updated: "TEE or Cardiac CT performed within 6 months prior to consent may be used to assess the Echo Exclusion Criteria. TTE or MRI may be used to assess some Echo Exclusion Criteria as applicable, however, neither TTE or MRI can be utilized as the sole imaging modality to assess the Echo Exclusion Criteria. If no historical imaging is available, imaging must be performed prior to randomization. If a significant cardiac event (potentially related to a change in cardiac status, e.g. CHF decompensation) occurs after cardiac imaging is obtained and before randomization takes place,	1. Safety Considerations	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	then imaging and should be repeated prior to randomization."			
9.2 Screening/Baseline Imaging	1. Revised to reflect imaging requirements at screening: **From:** **<u>Screening imaging must be performed prior to randomization.</u>** In sites without the appropriate CLAAS experience, Pre-Procedural Imaging Review supported by TEE or CT performed within 6 months prior to consent is required for the initial 5 subjects scheduled for implant. For subsequent patients, TTE, TEE, Cardiac CT OR MRI performed within 6 months prior to consent may be used to assess the Echo Exclusion Criteria. TTE or MRI may be used to assess some Echo Exclusion Criteria as applicable, however, neither TTE or MRI can be utilized as the sole imaging modality to assess the Echo Exclusion Criteria. If no historical imaging is available, imaging must be performed prior to randomization. If a significant cardiac event occurs after the cardiac imaging which causes a change in cardiac status [i.e., major Congestive Heart Failure (CHF) decompensation] the screening imaging must be repeated after informed consent and prior to randomization.	1. Edit for consistency with section 5 (schedule of assessments)	Y	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	To: **<u>Screening imaging (TEE or CT) must be performed prior to randomization.</u>** Imaging is required to assess the anatomic screening criteria. Cardiac CT or TEE can be used to assess all Echocardiographic Eligibility Criteria. TTE and MRI studies are limited to the assessment of Left ventricular ejection fraction and for detection of pericardial effusions. TTE and MRI cannot be used to assess other Echocardiographic Eligibility Criteria.			
9.3 Pre-Procedural Review	1. Updated to note historical imaging can be performed within 6 months of consent	1. Edits for clarification	N	N
9.5 Index Procedure	2. Added: "The TEE Baseline assessments will include review of the echocardiographic selection criteria to confirm these criteria have been met. In addition, LAA measurements will be obtained and reviewed to confirm sizing criteria in accordance with the CLAAS and Control System IFU."	1. Verify data collection is being completed in accordance with device IFU	N	Y
9.5.4 Intraprocedural Medical Therapy	2. Added prophylactic antibiotics to list of medication data collection.	2. Edits for clarification	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
9.5.7 Procedural Imaging	2. Added follow-up requirements for randomized and non-randomized subjects	2. Edits for clarification	N	N
9.7 Pre-discharge Follow-up	2. Added "Subjects are required to stay in the hospital at least 3 hours post-procedure." and "TTE is required to surveil for pericardial effusion. The study must be performed a minimum of 3 hours after discharge from cardiac catheterization laboratory."	2. Safety considerations	Y	Y
9.9 45-day Follow-up ± 7 Days (Telehealth Visit and Imaging)	1. Updated imaging requirements for 45-day Follow-up. "If TEE demonstrates a non-trivial pericardial effusion (defined as circumferential effusion measuring >10 mm), a TTE is required. Cardiac CT may be used. In cases where CT demonstrates the presence of a thrombus or a leak, a TEE is required to confirm and quantify findings." 2. Updated Concomitant Medications documentation requirements: "If DAPT has been interrupted or terminated, the stop date (and resumption date, if applicable) and the reason for interruption/termination should be recorded."	1. Safety considerations 2. Edits for clarification	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
9.9 45-day Follow-up ± 7 Days (Telehealth Visit and Imaging); 9.11 12-Month Follow-up ± 30 Days (Telehealth Visit and Imaging)	1. Revised to reflect imaging requirements for endpoint analyses **From:** Cardiac CT may be used in lieu of TEE. If a finding of Pericardial Effusion, Device Related Thrombus or inadequate seal is detected on Cardiac CT, a TEE is required to confirm finding **To:** Cardiac CT may be used in lieu of TEE to screen for end point findings, e.g., DRT or >3mm Leak. • If a Device Related Thrombus is detected, a TEE is required to confirm the finding as soon as possible (recommended assessment within 2 weeks; at latest, 4-6 weeks from date of original study or at the patient's next follow up visit, whichever is first). If a non-trivial leak is noted, a TEE is required to confirm the finding, as soon as possible (ideally within 2 weeks; at latest, 4-6 weeks from date of original	1. Edits for clarification; Safety considerations; Harmonization with section 5 (schedule of assessments)	Y	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	study or at the patient's next follow up visit, whichever is first). *Note: A trivial leak is one in which filling is incomplete or is seen on only delayed imaging, with a gap that is ≤1mm.* If a non-trivial Pericardial Effusion (defined as circumferential effusion measuring >10mm) is detected on Cardiac CT, TTE evaluation is suggested for quantification.			
9.12 Eighteen-month Follow-up ± 30 Days (Clinic Visit)	**Added:** 1. Subjects who had a procedure attempt but did not receive an implant must be followed through the Primary Endpoints with a minimum of telehealth/phone call visits at all visits including 7-days, 45-days, 6-months, 12-months, and 18-months (imaging not required and protocol mandated medication therapy not required). After the 18-Month follow-up, these subjects will have completed all required study assessments.	1. Consistency with sections 8.8.1-8.8.5	Y	Y

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
9.14 Suspected Stroke or Systemic Embolism Neurologic Events (Unscheduled Visit)	1. Updated assessment descriptions for Unscheduled Visits	1. Edits for clarification	N	N
11 Protocol Deviations	1. Corrected from "CRF" to "CFR" 2. Added: The use of waivers in this clinical study protocol is prohibited unless approval is received in writing from the Sponsor or designee. The Sponsor or its representatives will evaluate deviations to the clinical investigation plan during monitoring visits. Individual event corrective actions may be recommended at that time. In addition, deviations occurring across all investigational sites will be reviewed by the Sponsor or its representative on a periodic basis to determine if more global preventative actions may be required. The Sponsor may terminate an investigators or site's participation in the study (see Section 18.1.7).	1. Correction 2. EU MDR requirement in alignment with ISO 14155:2020	N	N
12 Safety Reporting	1. Formatting and definitions updated and compiled in table format for clarity	1. Edits for consistency and clarity	N	N
12.1 Reportable Events by Investigational Sites	1. Updated clinical events that are not considered reportable unless Principal	1. Edits for clarification	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Investigator determines that they are related to the investigational device or procedure, or an AE of special interest 1. Added language "and other regulations, as applicable" 2. Added language "and Conscious Sedation Sub-study Cohort"	2. Expanded section to reflect EU changes 3. Edits for clarification		
12.1 Reportable Events by Investigational Sites; 12.4 Unanticipated (Serious) Adverse Device Effect (UADE/USADE)	1. Updated from "Investigator" to "Investigator (or designee)". 2. Updated from "Sponsor" to "Sponsor (or Sponsor's representative)".	1. Edits for clarification	N	N
12.3 Device Deficiency	1. Following completion of the subject's 18 Month follow-up, adverse event collection will be limited to the following: • All serious adverse events • All device deficiencies	1. Edits for clarification.	N	N
12.4 Unanticipated (Serious) Adverse Device Effect (UADE/USADE)	1. Updated from: "The Sponsor will take the necessary steps to investigate the event and will be responsible for notifying FDA and all participating IRB/ REB/ECs (or other, as required) and all investigators." To: "The Sponsor will take the necessary steps to investigate the event and will be responsible for notifying FDA, other	1. Edits for clarification.	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	applicable regulatory authorities, and all other participating IRB/ REB/ECs (or other, as required) and all investigators."			
12.5 Serious Health Threat (SHT)	1. Added Section 12.1.7 Serious Health Threat.	1. Compliance with EU MDR requirement in alignment with ISO 14155:2020	N	N
12.6 Safety Event Reporting Timelines for Investigational Sites	1. Updated from: "The Investigator shall notify the Sponsor within 2 working days of first learning of any SAE using the eCRF." To: "The Investigator (or designee) shall notify the Sponsor, (or Sponsor's representative), within 2 working days of first learning of any SAE using the eCRF. If EDC is not available, the site should notify the Sponsor or Sponsor's representative via email, telephone or other correspondence within 2 working days of first learning of the SAE."	1. Compliance with EU MDR requirement in alignment with ISO 14155:2020	N	N
12.10 Benefit-Risk Assessment	1. Added: "This clinical investigation has been designed to comply with the requirements of EU MDR Chapter VI, Article 62 4(i), including the monitoring of risk as detailed in section 12.1.10."	1. Compliance with EU MDR requirement in alignment with ISO 14155:2020	N	N
14.5.1 Primary Effectiveness	1. Removed duplicative sentence: The primary effectiveness endpoint will be	1. Removed duplicative sentence	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	assessed with the following non-inferiority hypothesis:			
16.1 Data Collection and Monitoring	1. Added: "The EDC system will meet applicable requirements as set forth by FDA or other regulatory authorities. An audit trail will be available for tracking all data that the EDC user enters, modifies or deletes. The data entered into the EDC will be fully validated as described in the Data Management Plan and/or related documents, which may include using clinical investigation-specific range and consistency checks and database listings. Queries may be issued to the site via the EDC system and resolved by the investigator or his/her designee using the EDC. Data validation will be completed on a regular basis. The entire database will be re-validated to ensure that there are no outstanding data discrepancies prior to database lock. Any changes to the database after that time will require written agreement by the Sponsor."	1. Compliance with EU MDR requirement in alignment with ISO 14155:2020	N	N
16.4 Data and Record Retention; 18.4 Records and Reports	1. Updated Data and Record Retention period from "at least 15 years" to "at least 10 years or as specified in the	1. Data retention requirements vary by country	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	Clinical Trial Agreement and local regulations"			
17 Device Accountability	1. Added additional details regarding access, receipt, use, return, disposal, etc. of investigational devices.	1. EU MDR requirement in alignment with ISO 14155:2020	N	N
18.1 Applicable Regulations	1. Updated applicable regulations	1. EU MDR requirement in alignment with ISO 14155:2020	N	N
18.4 Records and Reports	1. Updated record retention requirements	1. EU MDR requirement in alignment with ISO 14155:2020	N	N
18.9 Clinical Trial Insurance	1. Added Section 18.1.9 Clinical Trial Insurance	1. EU MDR requirement in alignment with ISO 14155:2020	N	N
19.1 Selection of Study Sites and Investigators	1. Added: "Each site will have at least one delegated Echocardiographer willing and able to participate in the study."	1. Edits for clarification	N	N
19.2 Training of Investigators and Research Staff	1. Added additional acceptable methods of training 2. Added: "Investigators, Echocardiographers, and research staff listed on the Delegation Log who have completed study-specific training, will maintain essential documents as requested by Conformal and training documentation noting the training modules completed, and the date the training was completed."	1. Edits for clarification 2. Edits for clarification on delegation and training requirements	N	N
19.2.1 Specific Investigator Training Requirements	1. Added: "All participating implanting physicians will receive formal device	1. Edits for clarification on training requirements	N	N

Section(s) of Protocol	Description	Rationale for Change	Consent Change Y/N	EDC Change Y/N
	training prior to their first implant" and referred to the Manual of Operations for specified training requirements.			
19.2.2 Training Documentation	1. Added: "Other training requirements may be specified in the CONFORM Pivotal Manual of Procedures (MOP)."	1. Edits for clarification on training requirements	N	N
21.1 Appendix A: Definitions	1. Definition added for Patent Foramen Ovale [PFO] 2. Updated from "trivial" to "small"	1. Edits for clarification 2. Edits for clarification	N	N

Minor administrative changes related to formatting and consistency in terminology throughout the protocol were made.

Study Name/Study Number:	CONFORM Pivotal/21-101
Protocol Revisions Being Captured ***(Example: Rev A to B)***	Rev D to E

Section of Protocol	Description	Rationale for change	Consent Change Y/N	EDC Change Y/N
7.5 Control Devices	Added Boston Scientific's WATCHMAN FLX Pro to list of FDA approved LAAO control device.	Boston Scientific received FDA approval of the WATCHMAN FLX Pro (P130013/S057) on 06 Sep 2023.	N	N

	Title:	Document No.
conformal® THE SHAPE OF STROKE PREVENTION	CONFORM Protocol Summary of Changes	C-15
	Version 9.0	

Study Name/Study Number:	CONFORM Pivotal/21-101
Protocol Revisions Being Captured ***(Example: Rev A to B)***	Rev C to D

Item	Description	Section of Protocol	Rationale for change	Consent Change Y/N
Acronyms	Added F/U to define follow-up	1 Acronyms	Clarification of language in the protocol	N
Protocol Approval Page	Removed David Pomfret and added Karis Oasan	2.2 Protocol Approval Page	Updated to reflect changes within the organization	N
Study Contacts	Remove Yale Cardiovascular Research Center from Clinical Events Committee and added NAMSA and address	3 Study Contacts	Clinical Event Committee oversight has changed from Yale Cardiovascular Research Center to NAMSA.	N
Investigational Sites	Added up to 10 sites in EU and Central Asia; Locations of planned EU and Central Asia sites	4 Protocol Synopsis	Updated to reflect plan to initiate study sites in EU and Central Asia	N
Clinical Background	Added reference	6.1 Clinical Background – Atrial Fibrillation	Updated to reflect reference source.	N
Study Design and Rationale	Added general study timelines and milestones	8.2 Study Design and Rational	Updated to reflect general study timeline as per ISO 14155:2020.	N
Subject Population	Removed the word 'randomized'	8.7.2 Attempted Population	Updated to reflect the definition of a subject who meets the Attempt population criteria.	N
Index Procedure	Clarified windows for index procedure requirements for Randomized Cohort and Roll-In Cohort.	9.5 Index Procedure	Updated to reflect when LAA occlusion procedure should take place for the Randomized and Roll-In Cohorts	N

Item	Description	Section of Protocol	Rationale for change	Consent Change Y/N
Intraprocedural Medical Therapy	Removed requirement for prophylactic antibiotics, dose and timing	9.5.2 Intraprocedural Medical Therapy	Updated to reflect data collection requirements	N
Procedural Imaging	Removed ultrasound evaluation, added: A procedural ultrasound evaluation, e.g. TEE imaging)	9.5.4 Procedural Imaging	Updated to clarify the Imaging modality at the time of index procedure	N
Protocol Deviations	Added ISO 14155:2020, added statement regarding Investigator requirements and protocol deviation reporting at the Sponsor level.	11 Protocol Deviations	Updated to reflect requirements per ISO 14155:2020	N
Adverse Event Reporting	Updated the time of AE reporting for the Roll-In Cohort to be the time of consent	12.7 AE Reporting	Updated to reflect data collection requirements	N
Unanticipated Adverse Device Effects	Clarified method of reporting UADEs.	12.7.2 Unanticipated Adverse Device Effects	Updated to reflect methods of reporting UADEs to the Sponsor	N
Concomitant Medication Risks	Added statement that risks associated with concomitant medications related to LAAO index procedure may be outlined in the informed consent form, if required by local IRB or equivalent.	12.8 Expected Adverse Events – Risk/Benefit Analysis	Updated to reflect risks associated with concomitant medications may be requested by the overseeing and/or local IRB or equivalent reviewing body.	N
Data Management	Added statement The verification, validations and security of the EDC may be noted in the Data Management Plan and/or related documents.	16.1 Data Collection and Monitoring	Updated to clarify data management processes.	N
Corrective and Preventative Action	Added statement the Sponsor may assess if a corrective and preventative action plan is applicable to secure	16.1 Data Collection and Monitoring	Updated to clarify process for evaluation of non-compliances.	N

Item	Description	Section of Protocol	Rationale for change	Consent Change Y/N
	compliance. Immediate actions may be taken to secure compliance and should be documented.			
Data Retention	Added section to clarify study records shall be maintained for a period of at least 2 years or as otherwise noted in the site-specific clinical trial agreement.	16.4 Data and Record Retention	Updated to clarify data and record retention study requirements	N
IRB/REB/EC	Updated to include the Ethics Committee (EC) Added statement that The IRB/REB/EC may request additional requirements, in which case the Sponsor shall review and assess if implementation is applicable.	Updated throughout study protocol; 18.2 IRB/REB/EC	Included Ethics Committee per ISO 14155:2020.	N

Study Name/Study Number:	CONFORM Pivotal/21-101
Protocol Revisions Being Captured ***(Example: Rev A to B)***	Rev B to C

Item	Description	Section of Protocol	Rationale for change	Consent Change Y/N
Acronyms	Update acronyms table to reflect changes within the body of the protocol	1. Acronyms	Reflection of changed language within the body of the protocol	N
Primary Safety Endpoint	Update to clarify timeframe of major procedure-related complications which apply to the primary endpoint	4. Protocol Synopsis 8.3.1 Primary Safety Endpoint	Adjusted in response to study design considerations (SDC 1a, SDC 1b)	N
Secondary Safety Endpoints	Update to clarify the threshold(s) for non-inferior closure success.	4. Protocol Synopsis 8.3.3.3 Safety Effectiveness Endpoints with Statistical Hypothesis Testing	Adjusted in response to study design considerations (SDC 2)	N
Schedule of Assessments	Update to reflect changes as outlined the body of the protocol	5. Study Schema	Reflection of changed language within the body of the protocol	N
Eligibility Criteria	Updated Echocardiographic Exclusion Criteria #4 Updated to clarify typographical error in Inclusion Criteria #3 and Echocardiographic Exclusion Criteria #6.	4. Protocol Synopsis 8.5.1.1 General Inclusion Criteria 8.5.2.2 Echocardiographic Exclusion Criteria	Small pericardial effusion that presents as stable does not meet exclusion criteria. Clarification	N
Subject Classification	Update to further define subject classification for the consented population and intention to treat populations by cohort	8.7 Study Enrollment Process and Subject Classification and sub-sections 14.2 Analysis Populations	Clarification	N

Item	Description	Section of Protocol	Rationale for change	Consent Change Y/N
Screening/Baseline Assessments	Update to clarify collection of vital signs at baseline, imaging requirements, and neurological assessments Clarification of screening and baseline imaging. Addition of new screening requirements for sites without the appropriate prior CLAAS® experience Pre-Procedural Imaging Process	9.1 Screening/Baseline 9.2 Screening/Baseline Imaging 9.3 Pre-Procedural Review 9.5.4 Procedural Imaging	Clarification and new screening requirements per protocol. Modified in response to and in response to study design considerations (SDC 8).	N
Pre-Discharge Follow-Up	Update to clarify collection of vital signs	9.6 Pre-discharge Follow-up	Clarification	N
7-Day Follow-Up	Update to remove targeted history collection	9.7 7-day Follow-up	Clarification	N
45-Day Follow-Up	Update to remove targeted history collection	9.8 45-day Follow-up	Clarification	N
6-Month Follow-Up	Update to remove targeted history collection	9.9 6-month Follow-up	Clarification	N
12-Month Follow-Up	Update to remove targeted history collection	9.10 12-Month Follow-up	Clarification	N
18-Month Follow-Up	Update to remove targeted history collection, clarification of collection of vital signs	9.11 Eighteen-month Follow-up	Clarification	N
Annual Follow-Up 2-5 Years	Update to remove targeted history collection	9.12 Annual Follow-up 2-5 Years	Clarification	N
Suspected Stroke or System	Update to clarify personnel who may conduct neurological assessment in	9.13 Suspected Stroke or Systemic Embolism Neurological Events	SDC 8	N

Item	Description	Section of Protocol	Rationale for change	Consent Change Y/N
Embolism Neurological Events	the even of suspected stroke or systemic embolism. Update to clarify NIHSS evaluation.			
Adverse Event Reporting	Update to include device embolization. Update to include Device Related Thrombus.	12.7. Adverse Event Reporting 12.8 Expected Adverse Events – Risk/Benefit Analysis	SDC 6 Updated device-related risks to align with risk analysis	N
Inadequate Seal and Device Related Thrombus	Update to include instruction on patient-individualized antithrombotic therapy.	4. Protocol Synopsis: Antiplatelet and Anticoagulant Therapy Additional Considerations 9.5.6.1 Additional Considerations F.6. Anticoagulation/Antiplatelet Therapy Requirements – CLAAS	Modified to align with commercial DFU medication therapy	N
Statistical Analysis	Update to Effectiveness Endpoint of inferiority margin and justification. Update to the Analysis Populations to remove mITT, PP, AT and replace with Intended, Attempted and Implanted populations. Update to Primary Effectiveness to update one-sided confidence interval. Update to Primary Safety to test from 18 months (Day 547) to 12 months (Day 365) General formatting changes	14.1.1 Effectiveness Endpoint 14.2 Analysis Populations 14.3.2.1 Primary Effectiveness 14.3.2.2 Primary Safety 14.3.3 Additional Analyses	Adjusted in response to study design considerations (SDC 1a, SDC 1b, SDC 2, SDC 3, SDC 9)	N

Item	Description	Section of Protocol	Rationale for change	Consent Change Y/N
	Update to Additional Analyses to mITT, PP, AT and replace with Intended, Attempted and Implanted populations.			
Study Definitions	Update to/addition of applicable definitions: Attempted Population Atrial Septal Defect Device migration Device related thrombus ITT Randomized Population Pericardial effusion grading	Appendix A: Definitions	Reflection of changed language within the body of the protocol and adjustments in response to study design considerations	N

	Title:	Document No.
conformal® THE SHAPE OF STROKE PREVENTION	CONFORM Protocol Summary of Changes	C-15
	Version 9.0	

Study Name/Study Number:	CONFORM Pivotal
Protocol Revisions Being Captured ***(Example: Rev A to B)***	Rev A to B

Item	Description	Section of Protocol	Rationale for change
Public Release of Study and Results	Update document to include the NCT for the pivotal phase and clarify that the sub-study will have a separate NCT number	Cover page 4 Protocol Synopsis 8.2 Study Design and Rationale	Included as required
Acronyms	Update acronyms table to reflect changes within the body of the protocol	1 Acronyms	Reflection of changed language within the body of the protocol
Protocol Approval Page	Update to reflect change in contact personnel	2.2 Protocol Approval Page	Reflection of updated contact information
RCT	Clarified study design of the Randomized Clinical Trial and enrollment phases	4. Protocol Synopsis 8.2 Study Design and Rationale 8.7. Study Enrollment Process and Subject Classification and sub-sections	Adjusted in response to study design considerations (SDC 27)
Sample Size	Update language to clarify enrollment parameters for each phase of RCT trial (1600 subjects to be enrolled in the RCT)	4. Protocol Synopsis 8.2.1 Number of Required Subjects 8.7. Study Enrollment Process and Subject Classification and sub-sections	Adjusted in response to study design considerations (SDC 10, SDC 27)
Investigational Sites	Update to include expansion into Japan	4. Protocol Synopsis 6. Introduction 8.2.1 Number of Required Subjects	Adjusted in response to study design considerations (SDC 10)
Study Duration / Follow-up Period	Clarification of timepoint for enrollment and follow period	4. Protocol Synopsis 8.2.2 Estimated Enrollment Time	Clarification

Item	Description	Section of Protocol	Rationale for change
Primary Safety Endpoint	Update to clarify definition of the primary safety endpoint composite and testing method	4. Protocol Synopsis 8.3.1 Primary Safety Endpoint 12.1.2 Safety Endpoint 12.3.2.2 Primary Safety	Adjusted in response to study design considerations (SDC 1, SDC 3)
Primary Effectiveness Endpoint	Update to clarify definition and testing method	4. Protocol Synopsis 8.3.2 Primary Effectiveness Endpoint 9.3.14 12.1.1 Effectiveness Endpoint 12.3.2.1 Primary Effectiveness	Adjusted in response to study design considerations (SDC 23, SDC 29a, 29b)
Secondary Safety Endpoints	Additional endpoint to capture all SAEs that are either device or procedure related, and reorganization of previous endpoints based on new addition	4. Protocol Synopsis 8.3.3.1 Secondary Safety Endpoints	Adjusted in response to study design considerations (SDC 4, SDC 9)
Secondary Performance and Efficiency Endpoints	Update to clarify definition and align with Munich consensus document	4. Protocol Synopsis 8.3.3.2 Secondary Performance and Efficacy Endpoints 12.3.2.4 Specific Secondary Effectiveness Endpoints with Statistical Hypothesis Testing	Adjusted in response to study design considerations (SDC 20)
Secondary Effectiveness Endpoints with Statistical Hypothesis Testing	Update to demonstrate effectiveness of device with powered hypothesis-based secondary endpoint comparing the two randomized arms for both procedure success and effective closure at 45 days (testing for non-inferiority followed by superiority)	4. Protocol Synopsis 8.3.3.3 Secondary Effectiveness Endpoints with Statistical Hypothesis Testing 12.3.2.4 Specific Secondary Effectiveness Endpoints with Statistical Hypothesis Testing	Adjusted in response to study design considerations (SDC 2, SDC 14)
Antiplatelet and Anticoagulant Therapy	Update to definition of anticoagulation therapy medication	4. Protocol Synopsis 8. Study Design 9.3.1 Pre-Procedure Medical Therapy	Adjusted in response to study design considerations (SDC 7)

Item	Description	Section of Protocol	Rationale for change
		9.3.2 Intraprocedural Medical Therapy 9.3.6.2 Antiplatelet and Oral Anticoagulant Therapy Requirements (CONTROL) 9.3.14	
Inadequate Seal	Update to reflect continuation of oral anticoagulants mandate if there is an inadequate seal as defined in the protocol until resolution of the leak/DRT are confirmed by TEE	4. Protocol Synopsis 9.3.6.1 Post-Procedure	Adjusted in response to study design considerations (SDC 8)
Schedule of Assessments	Update to reflect changes as outlined the body of the protocol	5. Study Schema	Reflection of changed language within the body of the protocol, and adjusted in response to study design considerations (SDC 6, SDC 22)
Current Standard of Care	Update to clarify limitations of current commercially available LAA closure devices, and published stroke risk for patients with AF data	6.2 Current Standard of Care to Treat Atrial Fibrillation	Adjusted to reflect most current data available
Investigational Device Use	Update to provide current summary and supporting details of the CLAAS device use to date	6.3 Conformal Prague Study 6.4 US Early Feasibility IDE Clinical Study	Adjusted to reflect most current data available
Control Devices	Clarification that a newly available control device will be added and included in an updated protocol, as applicable	7.5 Control Devices 11.1 Executive Committee	Adjusted in response to study design considerations (SDC 19)
Study Success	Clarification of study success definition	8.3 Study Endpoints	Adjustment in response to study design considerations (SDC 2, SDC 20)
Eligibility Criteria	Clarification that the RCT design is adequate to characterize the safety and effectiveness of the investigational device	8.4.2 Enrollment of Medicare Beneficiaries	Clarification in response to study design considerations (SDC 16)

Item	Description	Section of Protocol	Rationale for change
	while appropriately supporting the CMS criterion for coverage		
Subject Classification	Update to further define subject classification for the consented population and intention to treat populations by cohort	8.7 Study Enrollment Process and Subject Classification and sub-sections 12.2 Analysis Populations	Adjustment in response to study design considerations (SDC 30a, 30b, and 30c)
Screening/Baseline Assessments	Update to clarify parameters for lab values collected and assessments performed	9.1 Screening/Baseline	Adjustment in response to study design considerations (SDC 6, SDC 25)
Randomization	Clarification of parameters for randomizing consented patients	9.2 Randomization (RCT Cohort Only)	Clarification and adjustment in response to study design considerations (SDC 9)
Post-Procedure/Pre-Discharge Assessments	Update to discharge parameters, including a neurological assessment as part of the pre-discharge subject evaluation	9.3.7 Pre-discharge Follow-up	Adjustment in response to study design considerations (SDC 22)
Neurological Assessment Follow-up	Update to clarify stroke/TIA events assessment and follow-up parameters	9.3.14 Suspected Stroke or Systemic Embolism Neurologic Events (Unscheduled Visit)	Adjustment in response to study design considerations (SDC 7, SDC 24, SDC 26)
Adverse Event Reporting	Update to clarify timeframe and other parameters with regard to adverse event collection	8.7 Study Enrollment Process and Subject Classification and sub-sections 10.7 Adverse Event Reporting	Adjustment in response to study design considerations (SDC 9, SDC 21)
Clinical Events Committee	Update to clarify CEC adjudication process and blinding	11.2 Clinical Events Committee (CEC) 12.4 Measures to Minimize Bias	Adjustment in response to study design considerations (SDC 5)
Statistical Analysis	Update to clarify plans or handling missing data, poolability, sub-group analyses, and sensitivity analyses are outlined in a statistical analysis plan	8.3.3.3 Secondary Effectiveness Endpoints with Statistical Hypothesis Testing 12 Statistical Analysis Plan 12.3.2 Study Hypothesis and sub-sections 12.3.4 Poolability and Subgroup Analysis 12.3.5 Missing Data Handling	Adjustment in response to study design considerations (SDC 11, SDC 12, SDC 13, SDC 14 SDC 29b)

Item	Description	Section of Protocol	Rationale for change
Monitoring of data	Clarification that all study endpoints will be 100% source data verified	14.1 Data Collection and Monitoring	Adjustment in response to study design considerations (SDC 28)
Conscious Sedation Sub-Study	Update to re-organized and clarify the conscious-sedation sub-study with regard to study design and analysis	8.2 Study Design and Rationale Appendix A Definitions Appendix E Conscious Sedation Sub-Study Protocol	Adjustment in response to study design considerations (SDC 31a, 31b, 31c, 31d)
Study Definitions	Update to applicable definitions	Appendix A Definitions	Reflection of changed language within the body of the protocol and adjustments in response to study design considerations (SDC 3a, 3b, 3c, SDC 20, SDC 31b